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EXPERIENCES WITH CHEST WOUNDS FROM THE PACIFIC COMBAT AREA*

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WOUNDS OF THE CHEST, particularly in military quarters, provide unique and difficult problems for the medical personnel in transportation, treatment, and convalescence. The obvious vulnerability of the chest, the fatal potentialities of large sucking wounds, the quick fatality of injuries to the heart and large vessels, are all reflected in the high mortality from these causes on the battlefield, estimated to lie between 30 and 40 per cent.

Few reports are as yet available as to the incidence or severity of chest wounds in this war. Ferguson, *et al.*[1] have reported their experiences in transferring patients from evacuation to base hospitals in the South Pacific area. Among 4,039 patients there were 75 cases of chest injuries: One died following a pulmonary embolism; two sucking wounds required operative closure; hemothorax was left severely alone, aspiration being performed only when respiratory embarrassment demanded it, or when the clinical picture suggested the possibility of infection. They stress the frequent development of temperature as high as 103°F. in the presence of a sterile hemopneumothorax, persisting as long as two weeks. They were emphatic in their belief that the local use of the sulfonamides had made radical wound débridement unnecessary.

This conservatism in thoracic injuries among our naval surgeons finds confirmation in the experiences of British surgeons in desert warfare.[2] Among 2,500 battle casualties not a single operation was performed primarily to deal with a wound of the chest. The removal of foreign bodies was delayed until the patients reached a base hospital. Aspiration was employed only to relieve mediastinal shift or respiratory difficulty. Of 63 penetrating wounds of the chest only three developed empyema. Conservatism in front-line thoracic surgery was advocated.

In contrast to these experiences from the combat zone, Schrire,[3] an

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English surgeon, recently stated that unless the condition of the patient was so bad as to render any operative intervention an entirely hopeless procedure, every patient with a penetrating wound of the chest admitted under his care was subjected to an exploratory thoracotomy as an emergency measure if seen within 12 hours after the injury. Similar views have been expressed by both military and civilian surgeons.[4]

With these expressions of conservatism and radicalism before us, it may be instructive to survey the course of events in a group of patients from the Pacific Combat Area, and to glean from illustrative cases some of the lessons they so pointedly teach. Any criticism that may be presented is directed not to individuals, but to us as teachers who have failed in our teaching.

The immediate care of wounds of entrance and wounds of exit often determines the final outcome. Bullet wounds are frequently small, appear perfectly clean, heal like surgical incisions, and after a month's time defy detection. Given such sharply cut wounds, a simple dressing should suffice. At other times, bullets, shrapnel and mortar fragments produce ragged, dirty-looking wounds, with severely traumatized edges, capable of acting as an excellent culture medium for the growth of organisms. Such wounds, if seen within six to ten hours, should be excised under local anesthesia, the raw surfaces smeared with a sulfonamide mixture of sulfathiazole and sulfanilamide, equal parts, and the skin edges loosely approximated. Four grams of sulfathiazole or sulfadiazine are given by mouth immediately, followed by one gram every four hours over a period of three to five days. If seen later than ten hours after the injury, without obvious infection, a cleansing débridement is performed and if there is no sucking wound, the tissues are not sutured, the raw surface being treated with sulfonamides and with a dressing of vaselined gauze.

Contrasting results in the following two simple through-and-through wounds of the chest illustrate the imperative need of early excision of devitalized tissue particularly of the wound of entrance.

Case 1, age 25, was shot through the left lower chest on board a battleship at sea on June 23, 1942. A simple dressing was applied. He was admitted to Mare Island Naval Hospital 60 hours later. His temperature was 102° F., pulse 140, respirations 35, and blood pressure 92/64. A foul-smelling discharge was already escaping from the wound of entrance, preventing any adequate débridement or closure at this late stage. Roentgenograms (Fig. 1a) revealed a left chest full of blood with displacement of the mediastinum to the right. 1400 cc. of blood was aspirated from the chest which, on culture, proved to be sterile. By July 1, however, the infection of the superficial wound had penetrated the hemothorax, producing a pyopneumothorax, and a sucking wound of entrance. The patient died on July 10, with a massive empyema, a mediastinitis, and an infarction of the right lower lobe. The left lung was completely collapsed.

Case 2, age 59, was shot through the left lower chest on July 1. He was immediately admitted to Mare Island Naval Hospital, where a débridement of the wound of entrance with closure of the skin edges was done at once under local anesthesia. Although roentgenograms (Fig. 2) showed a left chest full of fluid and a mediastinal shift to the right, there was little dyspnea, and so no aspiration was performed until August 20, over a month after the injury, when 1000 cc. of reddish fluid was aspirated. On Sep-

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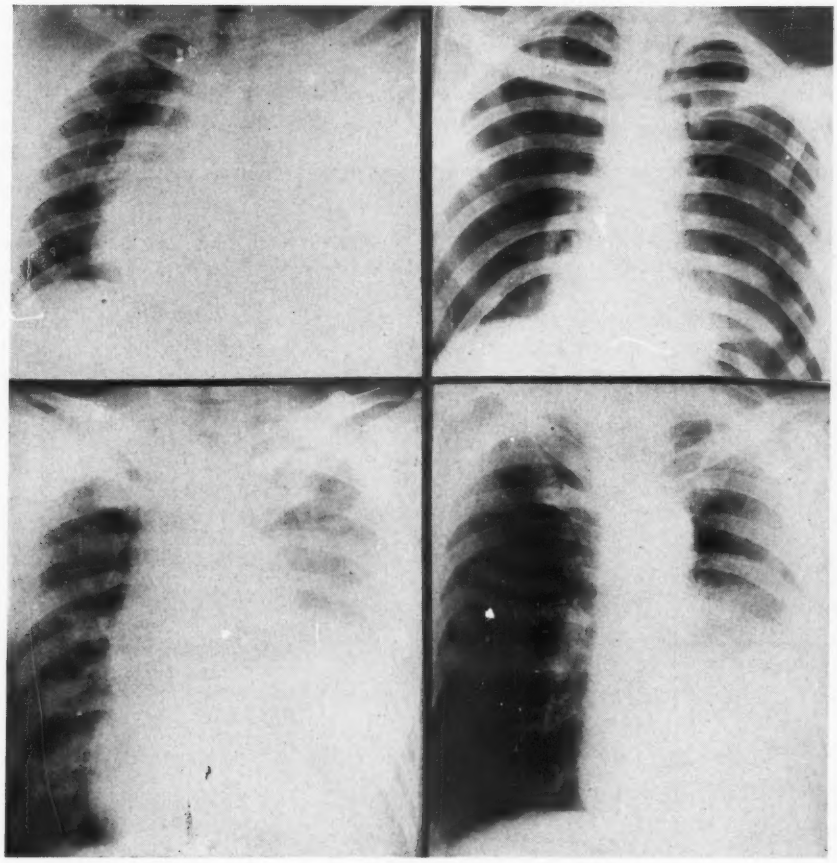

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FIG. 1.—Case 1: (a) Roentgenograms of gunshot wound of left chest showing massive sterile hemothorax on admission June 25, 60 hours after injury. (b) This was followed by a pneumopyothorax (July 1) and the death of the patient on July 10. Excision of wounds of entrance and exit had *not* been performed.

FIG. 2.—Case 2: Roentgenogram on July 1, 1942 following a through-and-through gunshot wound, with massive hemothorax and mediastinal displacement. Following immediate excision of wounds and three subsequent aspirations on August 20, September 9, and September 16, complete recovery occurred.

tember 9, 100 cc. was aspirated and on September 16, 375 cc. was obtained. He made an uneventful recovery and was discharged from the hospital on October 10.

Although these two injuries were almost identically located, and presented exactly similar immediate effects, the one in whom immediate excision and closure of the wound of entrance was performed recovered, while the other, in whom immediate excision was not performed, died of massive pleural empyema and mediastinitis, a direct extension from the superficial wound.

In the following case, failure to excise the traumatized tissue in the wound of entrance also led to a localized infection and subsequent extension of the infection to a hemothorax, resulting in a massive empyema. In this case, it seems probable that failure to perform a simple débridement at the time of

injury now makes a thoracoplasty necessary before complete healing can be expected.

Case 3, age 21, was injured August 9, 1942, by a piece of shrapnel which entered the right chest (Fig. 3), just below the clavicle, the fragment lodging posteriorly adjacent to the spine. There was an immediate paralysis of the right leg, which

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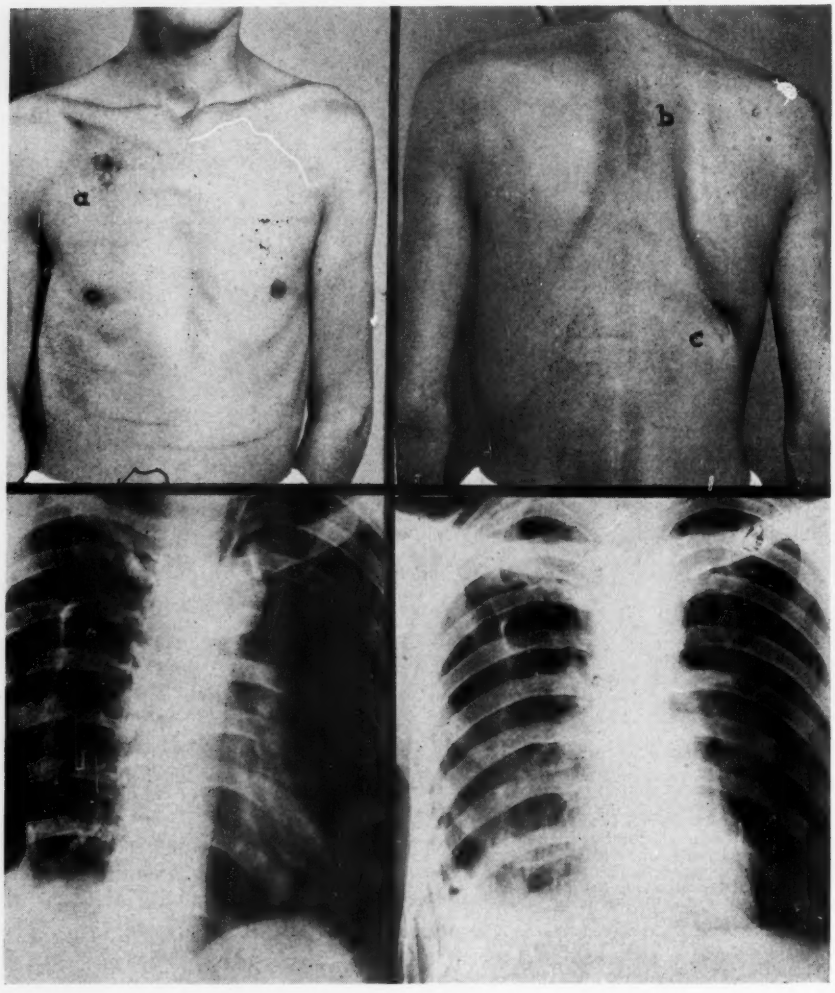

4a 4b

FIG. 3.—Case 3: Photograph on January 5, 1943; patient having sustained injury on August 9, 1942:

(a) Wound of entrance, now well healed, was *not* excised at time of injury.

(b) Operative site of removal of foreign body on November 20, 1942. Healing *per primam.*

(c) Resection of rib for empyema on September 18. The long interval between injury and the development of the empyema, and the sterile foreign body, suggest that infection occurred by extension from wound of entrance, and might have been avoided by early excision and closure.

FIG. 4.—Case 3: Roentgenogram on January 6, 1943, disclosing a large chronic empyema cavity which was still present on February 11 and also on June 6, 1943. Thoracoplasty will be necessary for elimination of this cavity.

slowly improved after the removal of the foreign body on November 20. The initial treatment of the wound consisted of a simple dressing, the administration of 0.5 cc. of tetanus toxoid, and 120 grains of sulfathiazole in five days, obviously an inadequate amount. On August 14, 250 cc. of serosanguineous fluid was aspirated from the right chest, and on August 18 an additional 250 cc. of serosanguineous fluid was aspirated. On August 29, 20 days after the injury, a free flow of thin red-tinged pus from the wound was recorded, and on this date a rubber tube drain was introduced into the anterior wound.

On September 18, six weeks after injury, a resection of the tenth rib was performed for a putrid empyema and the rubber tube drain then inserted was still in place on admission to Mare Island Naval Hospital on January 1, 1943. A roentgenogram on January 6 (Fig. 4) revealed a large chronic empyema cavity which improved slightly on constant drainage and forced expiratory exercises, but on June 6 the cavity was still as large as on February 11, 1943 (Fig. 4). A thoracoplasty will be necessary before healing can be expected. It seems highly probable from the sequence of events, that the empyema might not have developed if the original wound of entrance had been excised.

Wounds producing compound fractures of the underlying rib require a cleansing débridement, with removal of loose bone fragments. If a direct communication with the pleural cavity is created thereby, the wound should be closed—after sulfonization—preferably by overlapping of available chest wall muscles without tension. Large sucking wounds require an immediate débridement and closure of the opening, if possible. When first seen on the battlefield such a wound (after sulfonization) may be closed with massive dressings, or with a sterile glove over the opening, and with a tight adhesive bandage encircling the chest. At the first opportunity such wounds must undergo a cleansing débridement, with removal of fragmented ribs, foreign bodies, and blood clots within the chest cavity. Sulfonamides are applied to all exposed pleural surfaces, and the defect in the thoracic wall loosely closed. In the event of obvious gross contamination of the pleural cavity with clothing or actual dirt, a mushroom catheter should be placed in the first intact intercostal space below the wound, the catheter being closed with a clamp until underwater drainage is established at the patient's bedside.

Considerable ingenuity may be necessary to close the defects in the thoracic wall depending upon their location and size. Defects in the lower chest, as for example, below the level of the dome of the diaphragm, may be closed by stitching the diaphragm to the parietal pleura at the upper border of the defect, the diaphragm having been previously paralyzed by transpleural crushing of the phrenic nerve as it courses over the pericardium.

The muscles of the thoracic wall such as the pectoral, latissimus dorsi, and trapezius, should, when possible, be approximated by overlapping, thus providing two lines of suture. Relaxing semilunar incisions in the muscle well away from the defect may be made, on one or both sides, depending upon the ease with which the muscles are approximated. There should be sufficient relaxation of the muscle to permit some overlapping and approximation without tension. If no muscle is available, subcutaneous fat and fibrous tissue may serve as one layer and skin as the second. When skin alone is

available, semilunar relaxing incisions may be necessary, on one or both sides, to effect closure without tension. The raw surfaces thus produced may be skin grafted immediately or be covered by vaselined gauze or sterile cellophane. A firm, voluminous dressing well strapped in place by adhesive plaster encircling the chest should be applied and not changed for seven to ten days in the absence of indications to the contrary. The sutures approximating contaminated muscle and subcutaneous tissues must be most gently applied and loosely tied to avoid excessive strangulation and pressure necrosis of included tissues. Such necrotic tissue serves as an admirable culture medium for the growth of bacteria, and all too frequently is responsible for the breaking down of sutured wounds.

When muscles are absent at the site of the defect in the thoracic wall, the resection of one or two ribs, on one or both sides of the defect, will permit closure of the now more mobile soft parts.

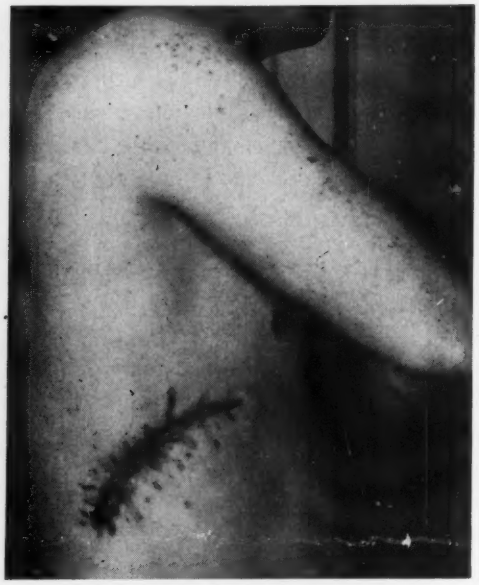

FIG. 5.—Case 4: Photograph of chest injury closed by suture to control sucking wound. Complete healing followed a late sequestrectomy of rib. Despite a massive hemothorax (Fig. 6) no pleural infection occurred.

Case 4, age 20, on September 25, 1942, sustained a severe wound of the right lower chest from a machine gun bullet which tore out a part of the thoracic wall producing a sucking wound. The wound was temporarily closed by heavy dressings and he was given 1000 cc. of plasma, having lost a great deal of blood both to the outside and into the chest. He was flown by plane to an advanced base where a cleansing débridement and closure of the wound were performed on about the fourth day (Fig. 5).

A roentgenogram (Fig. 6a) on the day following the injury showed a large hemothorax and fractures of the 8th, 9th, and 10th ribs.

Closure of the wound was followed by a late osteomyelitis of the rib, which necessitated a sequestrectomy on December 5, 1942, after his arrival in the U. S. A. Complete healing of the wound followed, but complete comfort was not attained until several focal spots of pain in the scar were injected on two occasions with 50 cc. of 1% novocain.

HEMOTHORAX

Of 36 cases of thoracic injury admitted to Mare Island Naval Hospital, 19 had been complicated by a massive hemothorax. In some cases multiple aspirations had been found necessary, a total of 27 aspirations having been performed in 12 cases. In seven instances complete recovery occurred without aspiration. Four of the 12 cases aspirated were complicated by empyema

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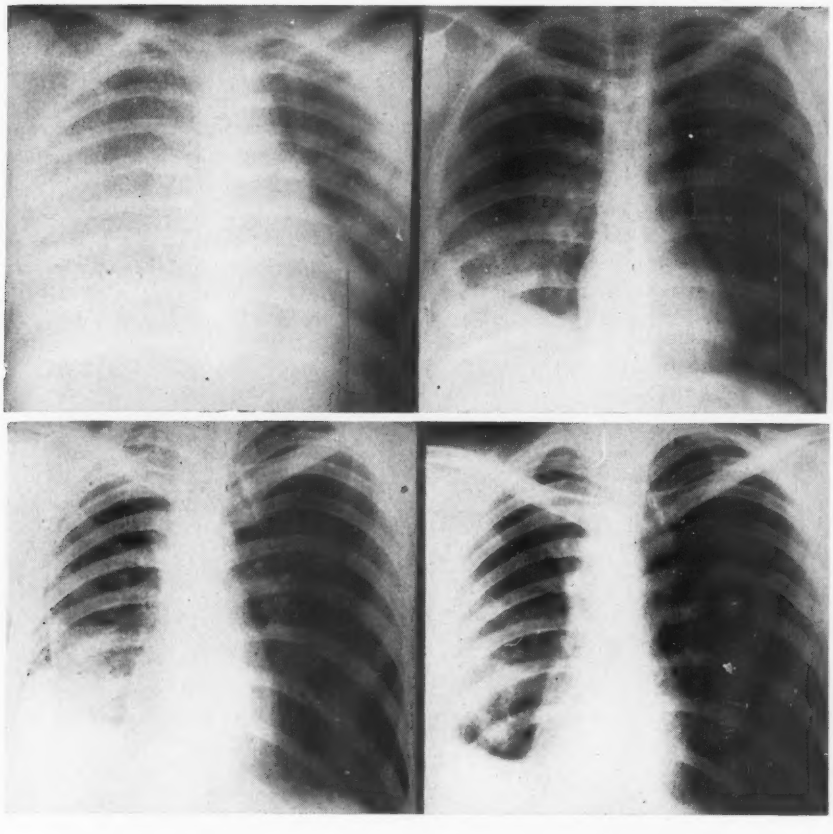

7a 7b

FIG. 6.—Case 4: Roentgenograms of chest: (a) In the presence of a hemothorax following a sucking wound controlled first by large firm dressing and then by operative closure of the wall.

(b) Two months later showing almost complete clearing of chest without intervening aspiration.

FIG. 7.—Case 5: (a) Roentgenogram on January 28 showing a large pyopneumothorax following aspiration of blood and air replacement 16 days after injury, which occurred on October 24, 1942. Air replacement unnecessary at this late date.

(b) Drainage and forced expiratory exercises were followed by expansion of lung and obliteration of empyema cavity.

(Cases 1, 3, 5 and 6), two of these aspirations having been supplemented by air replacement.

Case 5, age 20, was wounded by a machine gun bullet on October 24, 1942, producing fractures of the right 6th, 7th, and 8th ribs and of the body and neck of the right scapula. He immediately found breathing difficult and coughed up bright red blood. A roentgenogram on October 29, five days after injury, revealed a "right hemothorax with marked compression of the lung, and shift of the mediastinum to the left." However, there was no marked difficulty in breathing, and not until November 9, *16 days after the injury*, was aspiration considered necessary. At this time his temperature was 103° F., pulse 120, and respirations 40. 720 cc. of old blood was aspirated from the right chest on November 9, and *an equal volume of air reinjected*, for what purpose the record does not state. On the following day he was greatly improved but on November 17 his temperature again rose to 104° F., and on this

date 500 cc. of bloody pus was removed by aspiration. Two days later drainage was established by resection of the 8th rib. He was admitted to Mare Island Naval Hospital on January 25, 1943, with the drainage tube still in place. Roentgenograms revealed a pyopneumothorax of considerable extent (Fig. 7). Forced expiratory exercises with the tube in place were continued hourly each day until February 9, when the tube was permanently removed. A roentgenogram on March 15 showed good expansion of the lung and obliteration of the empyema cavity. Except for a mild osteomyelitis of the scapula with discharge of several sequestra he has made a complete recovery (Fig. 8).

Case 6, age 24, was wounded by machine gun fire on January 19, 1943, resulting in a small wound of entrance at the medial end of the left clavicle, and a large, jagged, sucking wound of exit in the left axilla. Marked dyspnea and hemoptysis occurred immediately. Under local anesthesia, a cleansing débridement of the axillary wound was undertaken at once, and the opening closed with muscle and fascial sutures. When

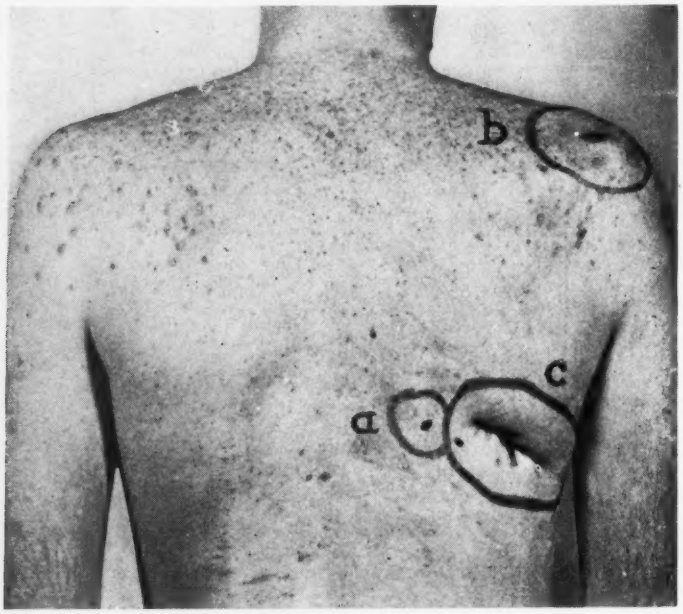

FIG. 8.—Case 5: Photograph February 16, 1943. Gunshot wound of chest, October 24, 1942, producing fractures of 6th, 7th and 8th ribs and a hemothorax. (a) Wound of entrance; (b) wound of exit; (c) healed operative wound for drainage of empyema.

this wound was closed the wound of entrance became a sucking wound, necessitating its closure by débridement and muscle sutures. Three transfusions were given in the next three days.

On January 24, *five days after injury*, 820 cc. of bloody, *thin* fluid was aspirated from the left chest with replacement by an equal volume of air. The reason for such replacement was not stated in the record. On January 31, 150 cc. of serous fluid was aspirated, and between this date and February 17 (Fig. 9a), three further aspirations were found necessary. On February 19, a portion of the 3d rib was removed anteriorly, and "the skin was sutured to the pleura to keep the wound open." (Note in the Health Record).

On admission to Mare Island Naval Hospital on April 5, the roentgenogram revealed a complete collapse of the left lung very much as shown in the roentgenogram of March 1, 1943, (Fig. 9b). Following forced expiratory exercises definite but

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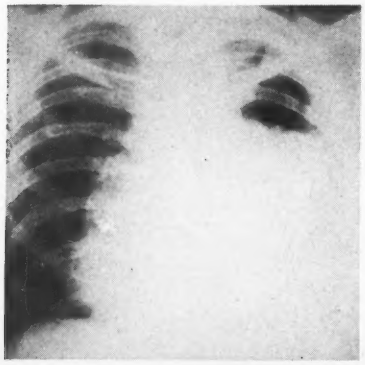
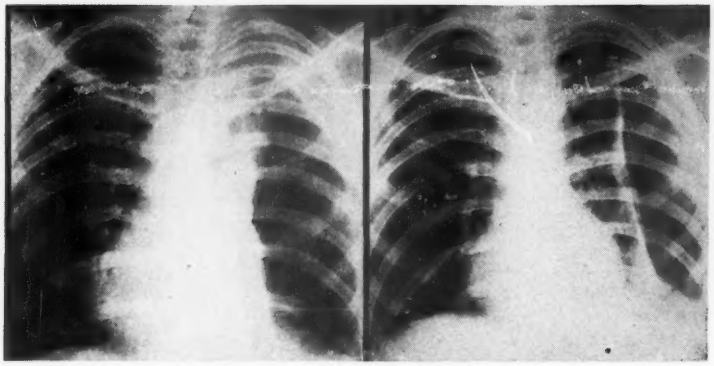


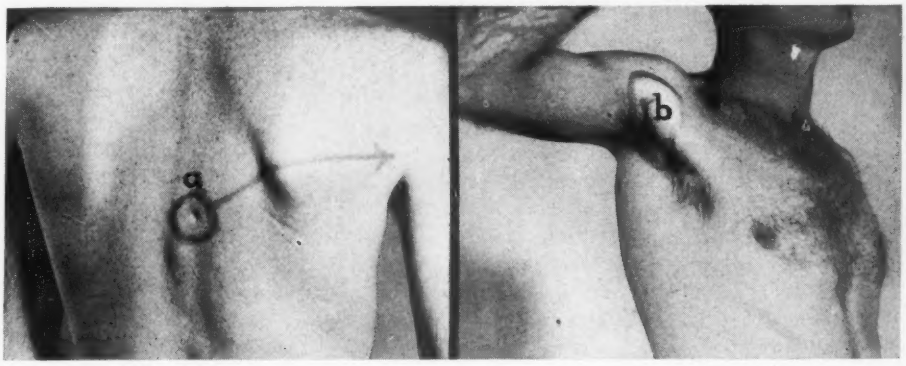


9b 9c

FIG. 9.—Case 6: Roentgenograms: (a) February 17, 1943, one month after gunshot wound and following five aspirations; the first aspiration being accompanied by replacement with 820 cc. of air. Massive pyopneumothorax still present for which rib resection was performed on February 19.

(b) Left lung completely collapsed, March 1, 1943.

(c) May 1, lung has only partially expanded, and a thoracoplasty will be necessary before complete healing can be expected, as improvement is now stationary.



10a 10b

FIG. 10.—Case 7: Rifle bullet wound producing massive pneumothorax. (a) Wound of entrance; and (b) wound of exit.

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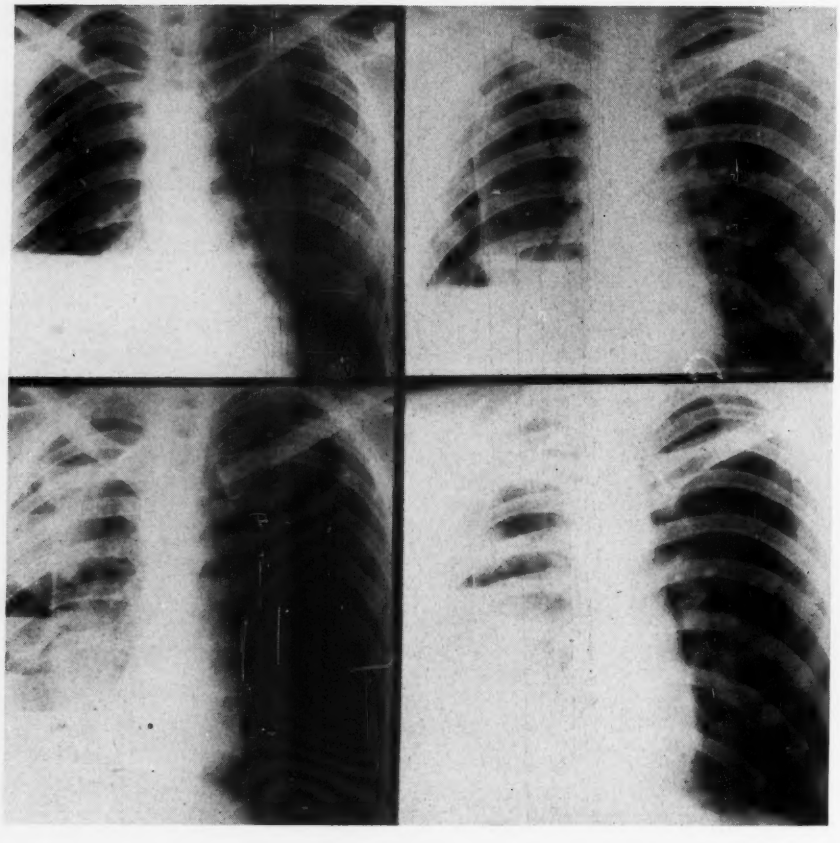

11c 11d

FIG. 11.—Case 7: Series of roentgenograms illustrating sequence of events following aspiration of sterile fluid and replacement with air on November 19, the original injury having occurred on October 7, 1942. Replacement with air was unnecessary and should not have been undertaken.

(a) Hemothorax three days after injury showing displacement of heart to left.

(b) Following aspiration of 1200 cc. of serosanguineous fluid and replacement with 1200 cc. air. Marked collapse of lung by pneumothorax.

(c) Three weeks later, showing marked pleural fibrosis.

(d) Another three weeks have passed with additional fibrosis and beginning shift of heart to right, pulled over by contraction of fibrous tissue.

incomplete expansion of the collapsed lung has occurred with diminution in the size of the empyema cavity (Fig. 9c). However, a thoracoplasty will undoubtedly be necessary before complete healing is effected, as improvement now seems stationary.

Case 7, age 30, was wounded on October 7, 1942, by a rifle bullet which entered the chest in back, to the right of the 6th dorsal spine and emerged in the right axilla (Fig. 10). Dyspnea, cough, and hemoptysis, and loss of motion in the fingers of the right hand were immediate symptoms, all of which gradually improved, although convalescence was complicated by causalgic pains in the domain of the median nerve. He was admitted to Mare Island Naval Hospital on November 13, about five weeks after the injury, with the original wounds almost healed, but with fluid in the right chest and a high temperature. On November 19, 1200 cc. of serosanguineous fluid was removed from the chest, *and replaced by an equal volume of air.* This replacement with air was unnecessary, and no explanation justifying it could be furnished by the

medical officer responsible except that he had read it was desirable. A culture of this fluid was found to be sterile. On November 24, 500 cc. of fluid and some air were aspirated. On November 27, blood smears were found positive for malaria, and the fever was attributed to it. On December 9, 160 cc. of fluid and considerable air were aspirated from the chest. Gradual improvement accompanied atabrine therapy for malaria, and by February 16, he was completely recovered.

Although replacement with air served no useful purpose whatsoever in this instance, it provided in a series of roentgenograms (Figs. 11 and 12) an instructive story of remarkable intrapleural fibrosis that followed an effusion and its aspiration. The subsequent contraction of this pleural fibrosis resulted not only in a reexpansion of collapsed lung, but it was sufficiently effective to cause a shift of the mediastinum and heart to the affected side. Definite evidence is provided in these roentgenograms that the obliteration of any empyema cavity is probably effected not only through active reexpansion of the lung by air, but also through fibrous contraction at the junction of the parietal and visceral pleurae, resulting in a gradual but steady pulling out of the lung.

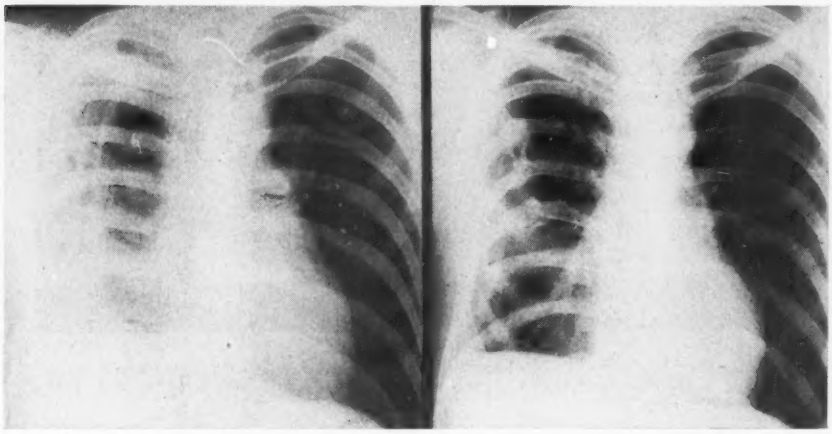

FIG. 12.—Case 7: Additional roentgenograms demonstrating gradual obliteration of previous pneumothorax by reexpansion of lung, but also by shift of mediastinum. By February 16, through contraction of pleural fibrous tissue, heart has assumed a midposition in the chest.

In five additional cases of hemothorax, aspirations were performed, removing as much as 1800 cc. of blood in one case, and 1100 cc. in another (Case 11), *without replacement with air.* Complete recovery without complication occurred in all cases.

Case 8, age 21, was struck by a machine gun bullet on December 7, 1941, the bullet entering the right chest anteriorly and emerging posteriorly directly opposite the wound of entrance (Fig. 13). He immediately became dyspneic, and complained of pain in his chest. Two days later he coughed up a small amount of dark red blood-tinged fluid. Gradual improvement occurred until December 23, when he complained of night sweats and headache, and he was found to have a fever. A roentgenogram on December 26 disclosed a right chest full of fluid (Fig. 14a). On January 2, 1942, 1200 cc. of bloody, thin fluid was aspirated, a culture of which was sterile. On January 7, 650 cc. of serosanguineous fluid was removed, and on January 14 only 100 cc. of fluid

could be obtained. Roentgenograms about five weeks later (Fig. 14b) showed practically complete clearing of the right chest, and he was discharged to full duty on March 10.

In seven cases of massive hemothorax without symptoms, complete recovery occurred without aspiration. The problem of aspiration of fluid from the chest has been subjected to much controversy, and unanimity of opinion and uniformity of procedure have not yet been achieved. As previously stated, American and British surgeons of this war have reserved aspiration for cases showing respiratory embarrassment, or for diagnostic purposes when empyema was suspected.

In the Military Surgical Manual[5] prepared by the National Research Council, the statement is made that "effusions extending above the sixth rib posteriorly are treated by aspiration and simultaneous replacement with air." Such a statement, however, requires many qualifications. A too literal acceptance of it will undoubtedly lead to much unnecessary aspiration, and the invariable replacement with air will certainly cause much retardation in

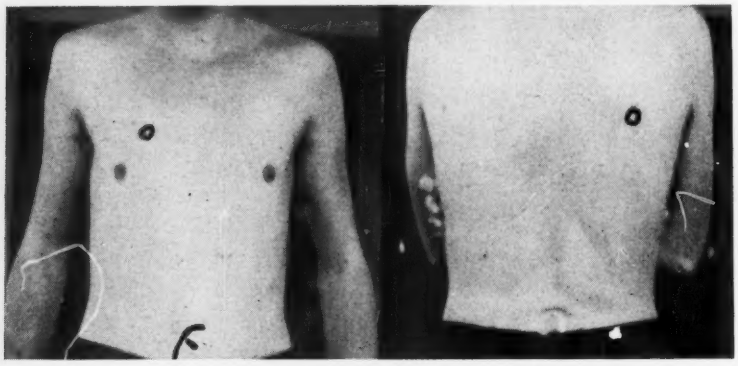

FIG. 13.—Case 8: Machine gun bullet passed directly through chest producing a massive hemothorax (Fig. 14). Bullet entered anteriorly at "o" and escaped posteriorly.

ultimate recovery. In many instances, effusions of this degree have given minimal symptoms, and have been completely reabsorbed. Moreover, the pressure of such an effusion is frequently a most effective preventive of further bleeding, and may be life-saving in the first 48 to 72 hours after the injury.

Should aspiration for dyspnea and respiratory embarrassment become necessary in these first few posttraumatic days, it would be advisable to limit aspiration to such an amount, probably 500 to 1000 cc., as would partially relieve the dyspnea. Studies of the aspirated fluid should be made to determine the hemoglobin content, the red cell concentration, and its sterility by culture. Should aspiration again become necessary because of dyspnea, or because of failure of absorption of remaining fluid, or because of its increase, or because of recurrence or increase in fever, the repetition of these studies of the aspirated fluid will reveal whether bleeding is continuing, as shown by a high hemoglobin and red cell concentration;

whether by dilution with fluid a clear effusion is developing; or whether by a great increase in leukocytes an empyema is present. If it is apparent that bleeding is continuing, another attempt at partial aspiration—this time accompanied by partial replacement with air—may be made before resorting to thoracotomy for control of the bleeding. If thoracotomy for bleeding becomes necessary, massive transfusions must be immediately available. An increasing clear effusion is best treated by repeated aspirations *without* air replacement.

An empyema developing at this early date is best treated by the introduction of a catheter in an intercostal space through a large trocar and cannula, the catheter being connected with a piece of rubber tubing long enough to establish an underwater seal beside the bed. At this early state a pneumothorax, such as would be produced by rib resection or intercostal incision, should be carefully avoided.

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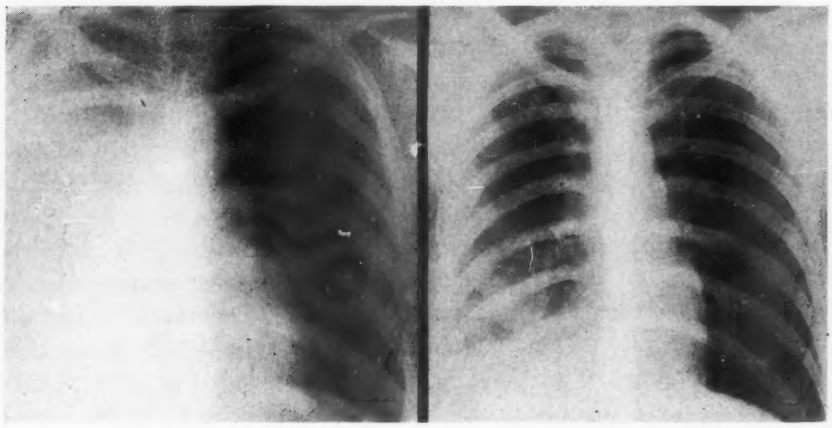

FIG. 14.—Case 8: (a) Roentgenogram showing right chest filled with fluid following through-and-through bullet wound on December 7. (b) Following three aspirations *without* replacement with air, chest became clear and patient was well.

The unnecessary replacement of aspirated blood or fluid with air may result in serious complications. The purpose usually advanced for such air replacement is that it maintains the collapse of the injured lung, and, therefore, the collapse of injured vessels likely to continue bleeding. But the pressure of a hemothorax should be as effective as a pneumothorax in the control of bleeding. Hemorrhage that cannot be so controlled will probably not be controlled by air replacement, although such an attempt at aspiration and replacement with air may be justified if aspiration alone has failed to control the dyspnea and bleeding. The danger of continued hemorrhage is ordinarily present only during the first 48 to 72 hours after the injury. After that time, thrombosis and fibrin deposits in the injured lung prevent further bleeding and make air replacement for the control of hemorrhage unnecessary. To replace with air the bloody fluid obtained by aspiration on

the *16th day* after injury as in Case 5, or even on the *fifth day* as in Case 6, is quite unnecessary from the point of view of continued bleeding. In both instances, a massive empyema developed. I do not suggest that replacement with air caused an empyema that would not otherwise have developed, but to say that aspiration and replacement with air prevent infection is not borne out by the facts. Moreover, it must be strongly emphasized that the cure of an empyema may be immeasurably complicated if the lung is already collapsed by a pneumothorax as the empyema develops. Air which replaces fluid tends to accumulate at the top of the pleural space, whereas fluid accumulates at the base. Therefore, infection of the pleural space in the presence of a pneumothorax may result in the fixation of the upper lobe in the collapsed state by inflammatory fibrosis of the visceral and mediastinal pleurae. This greatly complicates the subsequent elimination of the empyema cavity through inability of the lung to expand. In fact, in Case 6 the introduction of air greatly complicated subsequent recovery in that a massive empyema developed in the presence of a collapsed lung. If air replacement had not been instituted, the upper lung would in all probability have re-expanded, the upper visceral and parietal pleurae would have become adherent, the fluid remaining after aspiration would have tended to accumulate at the base, and the subsequent infection would have been limited to the lower thorax. Instead, a total empyema developed with complete collapse of the lung (Fig. 9), and a thoracoplasty is now necessary to eliminate the empyema cavity.

A most important consideration as to whether air shall replace aspirated fluid is the character of the fluid obtained. If a thin, bloody or serosanguineous fluid is obtained, bleeding has already ceased, and replacement with air will serve no useful purpose. It may be considered axiomatic that when thin, bloody fluid is obtained, as in Cases 6, 7 and 8, the aspiration of fluid need not—and should not—be accompanied by replacement with air.

A hemothorax without symptoms that is not aspirated is usually reabsorbed, occasionally in a surprisingly short time (Case 9).

Case 9, age 19, was shot, on October 5, 1942, by a rifle bullet which passed through the left chest. There was marked dyspnea but no hemoptysis. He was given three transfusions within the first week. A roentgenogram on October 26 showed a massive hemothorax extending above the 6th rib posteriorly (Fig. 15). On November 17, three weeks later, the blood had practically all disappeared, and the chest was clear. After a month's leave at home he was discharged to full duty on January 20, 1943.

Should a hemothorax without symptoms show no sign of diminution or reabsorption, an aspiration is in order at the end of the second or third week, to be repeated once or twice at short intervals until no further fluid is obtainable (Case 8). Replacement with air at this late date is unnecessary and should not be undertaken.

An occasional rare case may show massive clotting of blood which cannot be removed except by thoracotomy, which however must be justified by positive symptoms. On occasion, the removal of only a small amount of blood

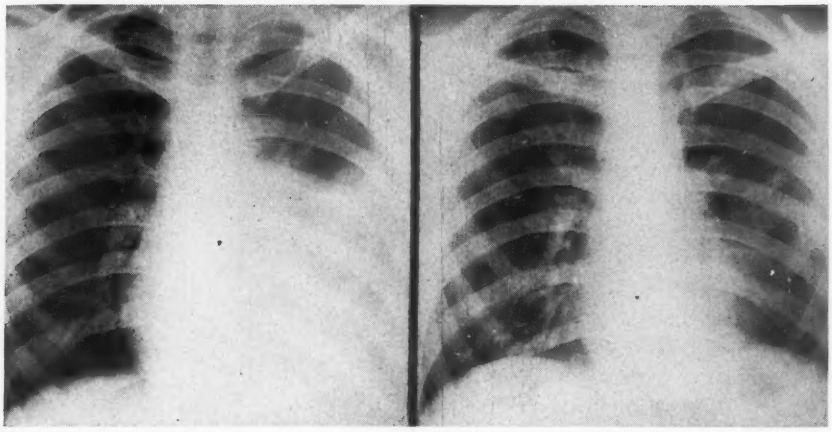

FIG. 15.—Case 9: Roentgenogram on October 26 shows a massive hemothorax following a through-and-through bullet wound on October 5. Roentgenogram on November 17 shows complete clearing of the lung and pleura without need of aspiration.

or fluid by aspiration may suffice to alter pressure relationships in the pleural space sufficiently to initiate absorption of the remaining fluid.

FOREIGN BODIES

The removal of foreign bodies may in most instances be deferred until the patient reaches a hospital in the continental United States, and their removal then depends largely upon their size, and upon whether the symptoms complained of may be attributed to their presence. Some surgeons consider missiles over one centimeter in size to be potential sources of later trouble and advise their removal. Such removal should be undertaken when ideal conditions prevail; when positive pressure or intratracheal anesthesia is available; and when accurate localization by fluoroscopy is possible. All foreign bodies in the chest should be examined under the fluoroscope by the surgeon himself, their exact location determined by the parallax method, and the two planes of location designated on the chest wall. In the absence of a Berman foreign body locator, this localization must be most accurately determined. Fluoroscopy, with a portable machine, may also be necessary to

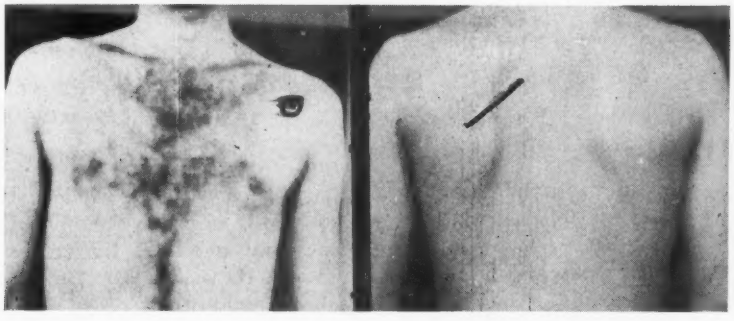

FIG. 16.—Case 10: Large fragment of shrapnel entered chest anterior to shoulder, traversed the lung and was removed through a posterior incision. Injury occurred on December 7, 1941, and fragment was removed on January 16, 1942.

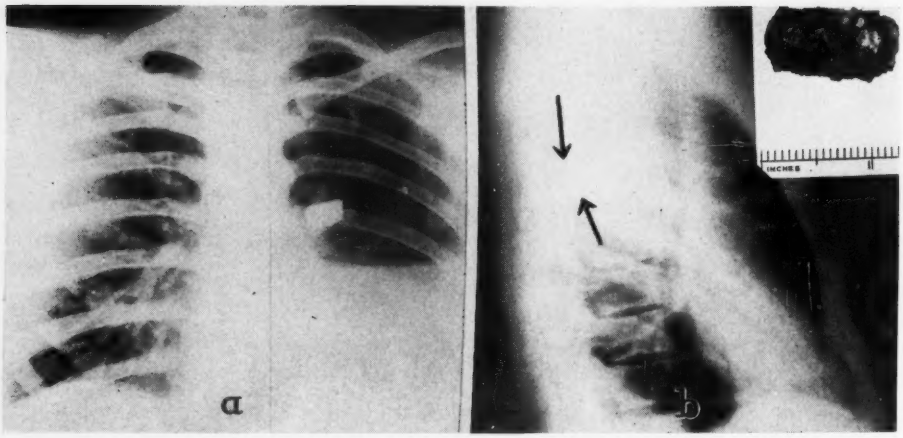

FIG. 17.—Case 10: Roentgenograms showing site of foreign body imbedded in lung. Insert shows fragment of shrapnel removed.

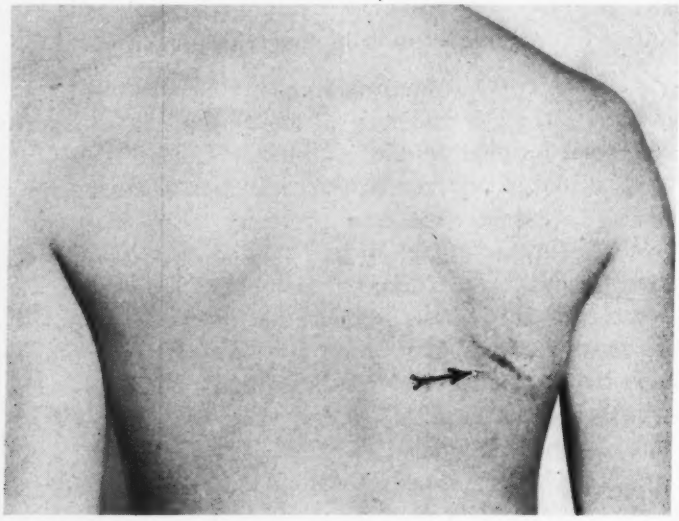

FIG. 18.—Case 11: The scar on right lower chest indicates site of wound of entrance on September 27, 1942 by a mortar fragment which traversed the lung and lodged in the middle lobe just posterior to 4th rib anteriorly. Late excision of the wound was performed on October 8.

find the foreign body at the operating table, after the lung has been exposed. Without these precautions, a surgeon may be extremely embarrassed by his unexpected failure to find the foreign body.

Case 10, age 23, was struck, on December 7, 1941, anterior to the left shoulder (Fig. 16) by a piece of shrapnel which lodged posteriorly near the spine opposite the sixth rib (Fig. 17). There followed an immediate paralysis of the left arm, marked dyspnea, pain in the chest and hemoptysis on several occasions. On December 16, a roentgenogram (Fig. 17a) showed fluid in the left chest to the level of the 7th rib posteriorly, but by January 13 (Fig.17b), the blood had all been reabsorbed. The patient complained repeatedly of pain in the chest on deep breathing and on exertion. Accordingly, on January 16, portions of the 5th and 6th ribs were removed close to

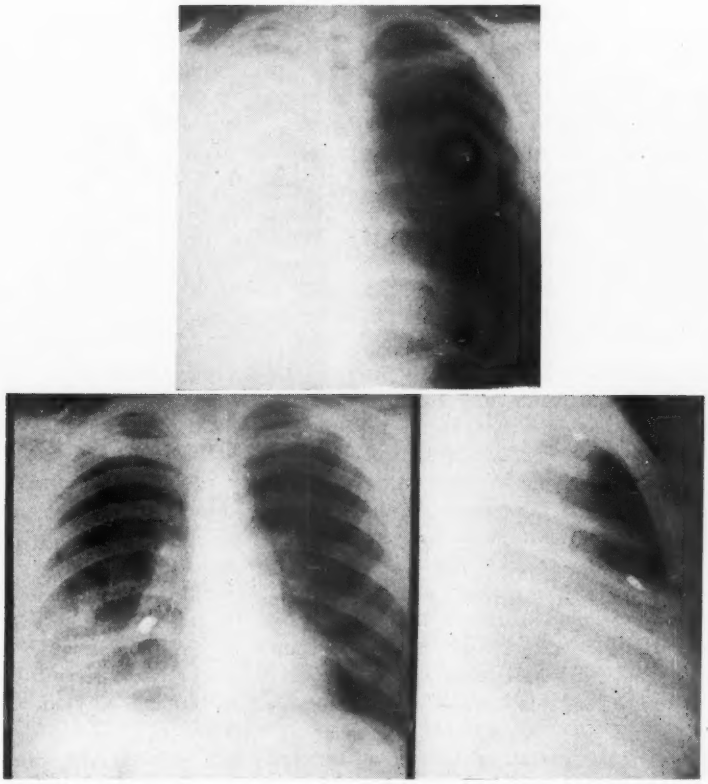

FIG. 19.—Case 11: Roentgenograms disclosing a massive hemothorax still present on October 26, following aspiration of 1100 cc. of blood on October 6 and 7. No more aspirations were performed, but absorption was practically complete on January 11, 1943. The shrapnel fragment was removed on May 10, 1943.

the spine, and the pleura was incised producing a partial collapse of the lung. The foreign body could not be felt nor seen, although there was an area of firm infiltrated lung about 10 cm. in diameter. Under fluoroscopy, the foreign body was more accurately located and the lung incised. A large jagged piece of shrapnel, 4 x 2.5 x 0.5 cm. was withdrawn from a fibrous-lined cavity. The cavity was curetted for other foreign material and the surfaces smeared with sulfathiazole and sulfanilamide, equal parts. The chest wound was closed without drainage. He was discharged to full duty on April 5, 1942.

Case 11, age 23, on September 27, 1942, was struck by a mortar fragment which entered the right chest in the back (Fig. 18) and lodged anteriorly in the middle lobe just posterior to the fourth rib. There was immediate hemoptysis, extreme dyspnea for three to four hours, and a soreness in the chest, accompanied by a subcutaneous emphysema. On October 6, 600 cc. of blood was aspirated *without air replacement,* and on the following day 500 cc. was aspirated, also without air replacement. On October 8, the wound in the chest wall was excised and resutured, followed by primary healing. A transfusion was given at this time. On October 26, a roentgenogram still showed a massive hemothorax obscuring most of the right lung field (Fig. 19) but no further aspirations were performed. A roentgenogram on January 11, 1943, disclosed a thickened pleura at the right lower base and the foreign body in the anterior chest. Because of the absence of symptoms, the patient was returned to full duty on January 13, 1943.

On April 25, the patient reentered Mare Island Naval Hospital complaining of pain in the anterior right chest, particularly after exercise and after long hours of duty. Accordingly, on May 10, the chest was opened through the fourth interspace anteriorly, the ribs being separated without division. There was no fluid, but a number of adhesions between parietal and visceral pleurae were disclosed laterally and anteriorly. Every care was taken *not* to separate these adhesions in order to avoid collapse of the lung. The foreign body could be felt in the substance of the middle lobe, surrounded by fibrotic lung. Two traction sutures were applied, the lung incised between them, the foreign body extracted from about 0.5 cm. below the surface, the cavity curetted for other foreign material, its walls smeared with the sulfonamides, and the incision in the lung closed by tying the traction sutures. The lung was inflated, and the incision in the lung tested for the escape of air by dropping water on the line of closure. No air escaped.

The chest wall was closed in the following manner: Two pericostal sutures of doubled No. 2 chromic catgut applied around the 4th and 5th ribs brought the two ribs closer together, but did not make them contiguous, since they had not been divided, and anteriorly they are normally widely separated.

The superior edge of the divided pectoral fibers was sutured to the inferior edge of the divided intercostal musculature with interrupted sutures of medium silk. The inferior edge of the divided pectoral muscle was sutured with interrupted silk sutures to the outer surface of the superior flap of the divided pectoral muscle, thus overlapping the first row of sutures. An air-tight closure was secured by this method of overlapping. The subcutaneous tissue was closed with interrupted silk, and the skin with a continuous suture of steel wire. Steel as a skin suture is desirable because it causes less reaction around stitch-holes than any other type of suture. An uneventful recovery followed, and the patient was transferred to a convalescent hospital on June 1.

Case 12, age 21, was struck on November 13, 1942, by shell fragments in the right chest posteriorly, in the left thigh and in the right hip. There was marked dyspnea and hemoptysis on two occasions on the day of injury. Plasma and tetanus toxoid were administered immediately, and sulfathiazole (quantity not stated) was given the following day. A roentgenogram on November 15 revealed a fractured 8th rib posteriorly, a small right hemopneumothorax, and a foreign body, 2 cm. in diameter, lying in about the center of the right upper lung field. He entered Mare Island Naval Hospital on January 30, 1943, with all wounds healed. Following leave, during which time he was operated upon for a ruptured appendix, he returned to the hospital in April complaining of discomfort in the right chest. Roentgenographically, the chest was clear except for the foreign body. Accordingly, the chest was opened through the second interspace anterolaterally. Numerous filmy adhesions between the visceral and parietal pleurae were carefully retained to avoid collapse of the lung. Palpation revealed the foreign body about 2 cm. below the surface of the upper lobe laterally under the second rib. Two traction sutures were placed in the slightly fibrotic lung and the lung incised between them. No attempt was made to control the bleeding that occurred except by digital pressure. The foreign body was removed from a fibrous-lined cavity, the cavity curetted for other foreign material, sulfonamides introduced, and the incision in the lung closed by a deeply placed, right-angled lock-stitch of chromic catgut on an atraumatic or swedged needle. The lung was inflated, and there was no escape of blood or air as tested by water dripping over the line of incision. The operative wound in the chest was closed exactly as described in Case 11. There was no postoperative subcutaneous emphysema, and the patient was discharged to a convalescent hospital on June 1, perfectly healed. Roentgenograms showed a completely inflated lung without pneumothorax.

The foreign bodies disclosed by roentgenograms in two other cases (Figs.

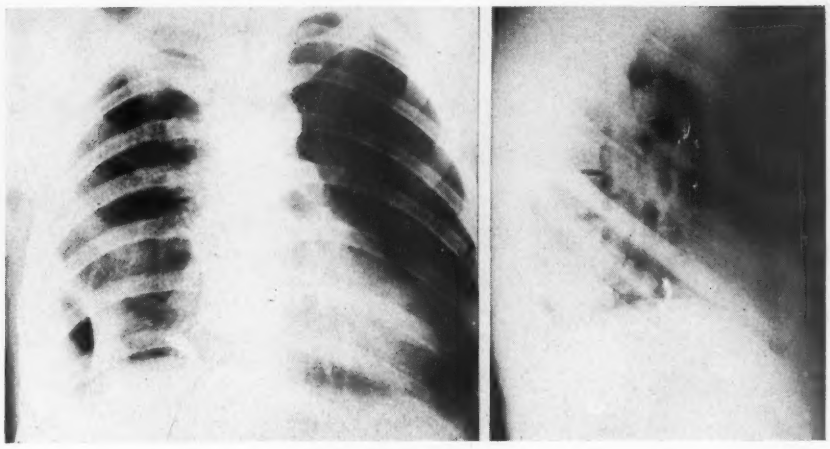

FIG. 20.—Roentgenogram showing shrapnel fragment in right lower midchest which has not been removed because of absence of symptoms. The empyema is cured.

20 and 21) were not removed because no symptoms accompanied their presence in the lung.

FOREIGN BODIES IN THE HEART

In 1939, Decker[6] made a thorough and complete review of the subject of foreign bodies in the heart and pericardium with a statistical analysis of 100 cases, 47 of which were operated upon, with a mortality of 17 per cent, and 53 of which were not operated upon, with a mortality of 30 per cent. Surgical opinion favors nonintervention when foreign bodies in the heart produce no symptoms. Some interesting and instructive experiences await the surgeons of this war, as the following cases illustrate:

Case 13, age 21, was struck on December 7, 1941, by shrapnel in the right chest,

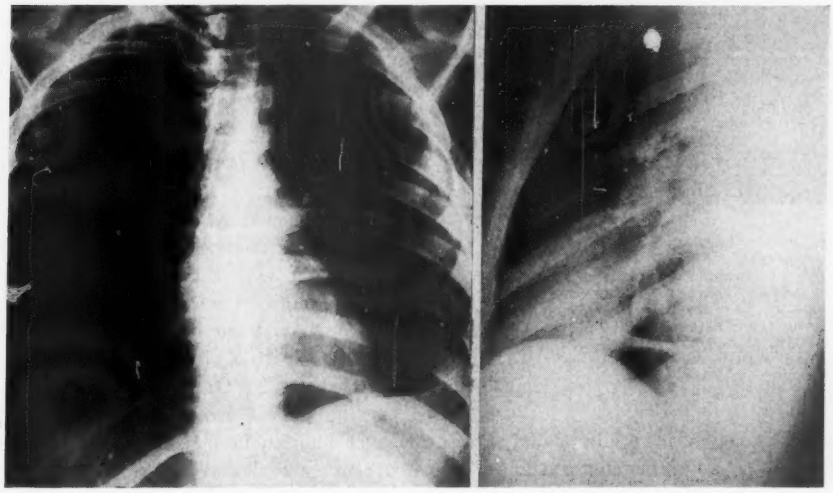

FIG. 21.—Roentgenograms showing multiple small foreign bodies in chest which have not been removed because they are symptomless.

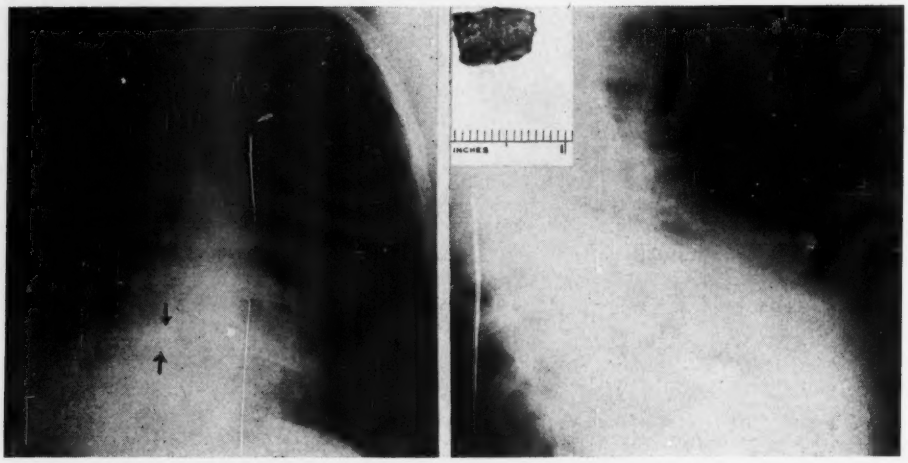

FIG. 22.—Case 13: Foreign body within pericardium, lying between the aorta and right auricle. The roentgenogram was interpreted as showing the foreign body in the lung. Fluoroscopy would have disclosed movement of fragment with each heart beat, thus locating it within the pericardium or within the heart.

the right elbow, and the right leg; followed by pains in the chest, difficult breathing, and dyspnea. Within two weeks all external wounds were well healed, and he had no complaints. On January 13, 1942, a roentgenogram (Fig. 22) revealed a moderate hemothorax, and a jagged foreign body lying 2 cm. to right of midline and about 3 cm. inside the chest. The size, weight, and jagged character of the fragment were thought to warrant its removal.

On January 23, 1942, the right chest was opened through a short incision paralleling the sternum, a portion of the fourth rib and cartilage being excised (Fig. 23). On opening the pleura no free fluid was encountered, but widespread filmy adhesions were found between the lower lobe and the parietal pleura. Palpation of the lung did not disclose any foreign body, and it was at once apparent that the trail of the shrapnel fragment led toward the heart, where it could be palpated within the pericardium. A large circular defect was seen in the right lateral surface of the midpericardium, about 2 cm. in diameter, filled with fibrinous exudate. This was enlarged toward the base, disclosing the origin of the aorta with a mass of fibrinous exudate overlying it, in which was embedded the foreign body. It appeared to lie at the base of the heart immediately between the aorta and the right auricle. The channel of entrance was enlarged by spreading it with a clamp. The fragment of shrapnel was withdrawn with considerable apprehension lest its removal be followed by bleeding. None occurred. A culture of the bed was taken, which subsequently proved sterile. One gram of sulfanilamide was placed in the pocket from which the piece of shrapnel was removed. The short, three-centimeter incision in the pericardium was not closed, so that any inflammatory fluid might escape into the pleural cavity instead of accumulating in the closed pericardium, thus producing a cardiac tamponade. The wound in the chest wall was closed in layers with cotton sutures, and an air-tight closure was obtained, followed by primary healing.

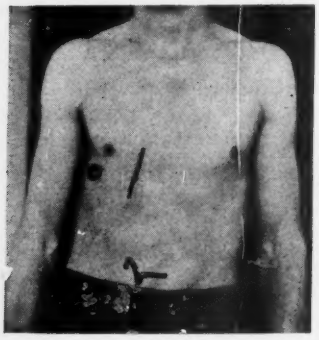

FIG. 23. — Case 13: The small circle marks the healed wound of entrance of shrapnel fragment that lodged within the pericardium at the base of the heart. The fragment was removed through a parasternal incision on January 23, 1942, the injury having occurred on December 7, 1941.

The postoperative course was uneventful except for several episodes of paroxysmal tachycardia accompanied by marked dyspnea, promptly relieved by an oxygen tent. He was discharged to duty, February 14, 1942, but three days later, he was readmitted with a temperature of 101° F., pulse 110-140, respirations 30, and pains in the right lower chest. Under simple bed rest and sulfathiazole all signs and symptoms slowly disappeared, and he was subsequently discharged to full duty.

Case 14, age 25, was wounded on December 7, 1941, by what subsequently proved to be a machine gun bullet, which entered the left chest posteriorly through a small inconsequential wound which healed in five days. There was no wound of exit, but a roentgenogram on December 10 failed to disclose any foreign body. He was returned to sea duty on the 8th day following the injury, but he soon noted attacks of faintness and dizziness, accompanied by sudden and momentary blacking out of vision, occurring with or without exertion, but particularly on climbing the ship's ladders, or when rising

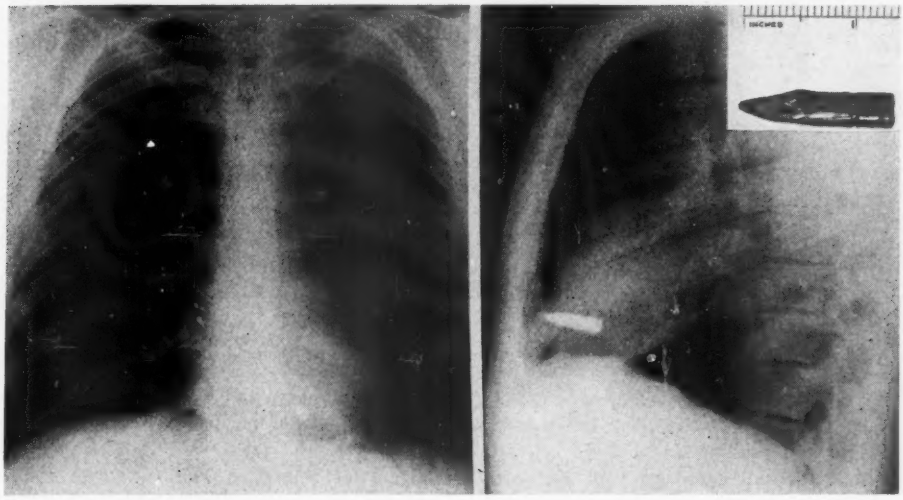

FIG. 24.—Case 14: Roentgenograms showing bullet (insert) imbedded in what subsequently proved to be the interventricular septum about 0.8 cm. below the surface of the myocardium. Injury occurred December 7, 1941. Bullet removed April 17, 1942.

suddenly from a sitting or stooping position. He remained on duty for 35 days, when he was transferred to the sick-bay of a destroyer tender with symptoms of nervousness, lack of appetite, loss of weight, increased sweating, and dizziness on standing up suddenly. He also experienced palpitations of the heart, dropped beats, and extra systoles. Physical examination was negative at that time, and his pulse and blood pressure were recorded as "normal." A diagnosis of "psychoneurosis and hysteria" was made and he was returned to duty.

However, he was unable to do his work and was transferred to another destroyer tender, where he had an attack of appendicitis for which he was operated upon at sea. Blood pressure on this occasion was recorded as 112/72. During convalescence, a roentgenogram was taken on March 7, 1942, disclosing a bullet in the heart. The radiologist's report follows:

"Fluoroscopy and films of the heart reveal the bullet to describe a dancing rotatory movement with each cardiac pulsation, the motion of the posterior end of the bullet being of slightly greater amplitude than its tip. With each pulsation it also moves upward toward the base about one-half centimeter. In all postures, right and left lateral, recumbent, prone, supine, oblique and exaggerated Trendelenburg, there is no shifting of position of the bullet, but the motions, synchronous with the heart

beats, remain constant. The size and contour of the heart are normal, and there is no evidence of free fluid in the pericardial sac; neither is there any residual evidence of pulmonary injury. The position and behavior of the bullet leads to the conclusion that it is at least partially imbedded in the myocardial muscle near the apex."

On admission to Mare Island Naval Hospital on March 30, 1942, he still complained of dyspnea on exertion, dizziness on assuming the erect posture suddenly, occasional sharp pains in the left chest, dropped beats and extra systoles. His color and nourishment were normal, temperature 98.6° F., pulse 88, respirations 18, blood pressure 110/70. There was a small oval healed scar on the posterior left thoracic wall, 3 cm. below the angle of the scapula. The heart was not enlarged. There was no murmur or friction rub to be heard, and the electrocardiogram was normal. A roentgenogram (Fig. 24) was interpreted as showing the bullet in the interventricular septum, in the region of the apex.

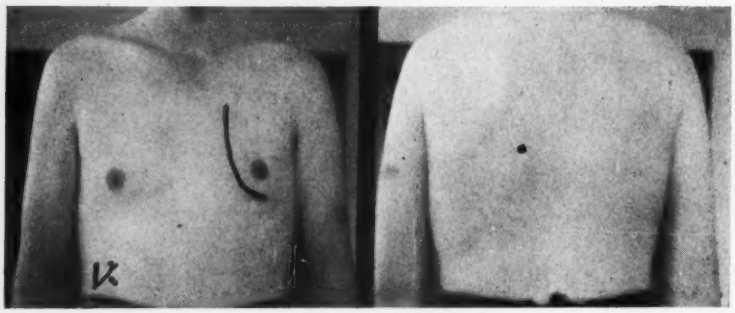

FIG. 25.—Case 14: Heart was approached through a curved incision; 8 cm. of 4th rib, and costal cartillages of 3rd and 5th ribs were removed. Pleural cavity was not entered. Dot on back shows healed wound of entrance of bullet which lodged in the heart.

On April 17, 1942, the bullet was removed. A curved incision was made to the left of the midline (Fig. 25). About 8 cm. of the 4th rib were removed together with its costal cartilage and the costal cartilages of the third and fifth ribs. The pleural cavity was not entered at any time during the operation. The pericardium, which appeared normal, was incised between two previously placed sutures. There were no adhesions, nor fluid in the anterior pericardial sac. In the midportion of the exposed anterior surface of the heart directly over the interventricular septum, was a round, discrete, elevated button of pink fibrous tissue 2.5 cm. in diameter, surmounted by a glistening endothelium, in the center of which could be felt the tip of the bullet lying about 8 mm. below the surface. The nubbin of fibrous myocardium was incised between traction sutures of cotton. The bullet lay encased in a tough fibrous wall about 1.5 mm. thick. This was incised and the bullet grasped with an Allis clamp. Traction on the forceps lifted the heart completely out of its bed, but failed to dislodge the bullet. Tugging on the bullet produced extreme irregularities in cardiac action. Several rather vigorous attempts at removal were unsuccessful. These difficulties were then surmised to be due to the creation of a vacuum behind the bullet. Accordingly, a grooved director was passed alongside the bullet, admitting air back of it, followed by prompt and easy removal. There was no bleeding. Sulfathiazole was introduced into the cavity from which the bullet had been removed, and the fibrous myocardium was closed with four interrupted cotton sutures. The pericardium was incompletely and loosely closed with two sutures so as to permit any blood or inflammatory fluid to escape into the mediastinum, thus avoiding the development of a cardiac tamponade. The wound in the chest wall was closed in layers with cotton sutures, without drainage.

An electrocardiogram, taken on the day of operation, instead of being normal as before, showed a sinus tachycardia, T1 was lower, and T2 had a late inversion.

On the day following operation the pulse was 105, and an electrocardiogram showed that T1 and T2 had become elevated. The conduction times were normal and unchanged. The T-wave changes were those seen with anterior myocardial abnormalities. The S-T intervals resembled those produced by pericarditis. On April 21 the electrocardiogram was again normal.

It was confidently hoped that this patient would be able to return to combat duty, but the symptoms of a war neurosis persisted, and it was necessary to discharge him from the service. However, at the present time he is without symptoms, has married, and is doing a full day's work in an aeroplane factory.

DISCUSSION AND SUMMARY

In 36 cases of gunshot wounds of the chest, 20 showed marked dyspnea, 16 hemoptysis, usually of very mild degree; 19 hemothorax, of which 12 were aspirated for a total of 27 times; 3 cases of aspiration were accompanied by replacement with air, 2 of which were complicated by empyema; 7 cases of hemothorax were not aspirated, followed by uncomplicated recovery; 8 cases had retained foreign bodies, in 5 of which they were removed; 8 had fractured ribs, for which no particular treatment was necessary; 6 had sucking wounds, requiring early closure; and 6 were complicated by empyema, 2 of which will require a thoracoplasty for cure. There were no deaths in the cases evacuated to the mainland from the South Pacific area.

The following principles underlie the treatment of thoracic injuries:

Clean-cut bullet wounds without symptoms require simple dressing only.

Jagged dirty wounds of entrance and exit should be excised immediately when possible, or filled with sulfonamide powder and excised later when the opportunity presents, if the wound is still free of pus.

Large sucking wounds of the chest must be closed, but such closure may tax one's ingenuity to the utmost. At the time of injury, if operative closure is not immediately possible, the wound or defect may be covered with a sterile rubber glove, or filled with sterile vaselined gauze, covered with a voluminous dressing, and fixed in place with a large adhesive bandage encircling the chest. This will produce fixation of the mediastinum which will permit the thoracoplastic procedures which later may be found necessary to close the defect.

Immediate available operative measures are:

Semilunar, relaxing incisions in the muscle layers either on one or both sides of the defect may permit closure of the muscles without tension.

Semilunar, relaxing incisions in the skin on one or both sides of the defect may permit closure of the defect. The resulting raw surfaces, away from the defect, may later be skin-grafted.

Resection of one or two ribs on one or both sides of the defect may permit sufficient mobilization of the soft parts to bring the tissues together without tension.

The liberal use of sulfonamides locally and orally is indicated in all instances. In case of gross contamination of the pleural cavity by dirt or clothing, drainage is indicated by air-tight catheter introduced through an intercostal space well separated from the closed wound.

Hemothorax is a frequent complication of gunshot wounds, but surprisingly often is not infected, and may be reabsorbed. The mere presence of a hemothorax warrants neither operation nor aspiration. Aspiration may be limited to cases showing respiratory embarrassment, to cases suspected of having a complicating infection, and to cases in which blood or fluid fails to be reabsorbed after two or three weeks. Increasing dyspnea in the first two or three days after injury may be evidence of continued bleeding. If degree of dyspnea and mediastinal shift demand it, aspirate as much blood as may be necessary to relieve but not to eliminate entirely the dyspnea, which must be controlled partially by morphine. The aspiration of a large volume of blood at one time is contraindicated as the sudden reexpansion of the lung may reactivate the bleeding. If dyspnea recurs promptly after simple aspiration, an attempt may then be made to secure relief through aspiration and replacement with air. Prompt recurrence of dyspnea after such an attempt demands thoracotomy for the control of the bleeding vessels. Before undertaking a thoracotomy to stop bleeding, massive transfusions must be available for immediate use.

A hemothorax or serosanguineous effusion that persists beyond two or three weeks without diminution may be aspirated, but replacement with air at this late date is not necessary. Thin, bloody fluid is evidence that bleeding has ceased, and that air replacement is unnecessary. Air replacement may be highly detrimental to prompt healing should an empyema develop in the presence of the pneumothorax. Extensive thoracoplastic procedures may be the penalty for unnecessary or ill-advised replacement with air.

Wounds of the lung do not require operative intervention *per se*, unless uncontrollable hemothorax or uncontrollable tension pneumothorax demand it. The removal of foreign bodies in the chest may be safely postponed in most instances until ideal conditions prevail. Positive pressure or intratracheal anesthesia should be available and exact localization of the foreign body by fluoroscopy should precede any attempts at removal, if the embarrassment of failure is to be avoided. Small, symptomless foreign bodies may be allowed to be retained without harm.

Linear wounds produced by débridement or simple incisions in the lung for removal of foreign bodies may be closed with deeply placed right-angled lock-stitch sutures of catgut on atraumatic needles. Leakage of air as demonstrated by dripping water over the line of suture must be controlled by reinforcing sutures.

Incisions in the myocardium may be closed with interrupted silk or cotton sutures. Following operations upon the heart, the pericardium should be closed very loosely with widely spaced interrupted sutures so as to permit escape of blood or inflammatory fluid that might, if retained within the pericardium, produce a cardiac tamponade.

Exploratory thoracotomy can usually be performed through intercostal incisions without rib division or rib excision if a suitable self-retaining rib spreader is available. When thoracotomy for the removal of foreign bodies

is performed, every effort should be made to avoid or limit the division of adhesions between the visceral and parietal pleurae in order to avoid unnecessary collapse of the lung. Such thoracotomy incisions may be closed air-tight by (1) pericostal sutures of doubled chromic catgut to approximate the ribs; (2) suturing superior edge of divided chest wall muscle to inferior edge of divided intercostal musculature; and (3) suturing inferior edge of divided chest wall muscle to outer surface of the superior flap of divided chest wall muscle, thus overlapping the first line of sutures. Interrupted sutures of silk or cotton should be used throughout. Continuous steel suture in the skin is preferable when available because of its nonirritating quality. Drainage is indicated only in the presence of marked soiling, as when thoracotomy is performed immediately following injury. Drainage by catheter connected with an underwater seal through an intercostal space independent of the thoracotomy wound is indicated.

Empyema developing in the first two to three weeks after injury should be drained by air-tight catheter rather than by resection of rib or intercostal incision, if at all possible, in order to avoid collapse of lung. Repeated aspirations and microscopic examination of the aspirated fluid will permit an early diagnosis of developing empyema when such catheter drainage can still be made effective.

Reexpansion of collapsed lung may be greatly accelerated by "forced expiratory exercises." The patient inspires deeply and then forcibly expires against a closed nose and closed mouth. Its effectiveness to produce expansion of the lung is easily demonstrated in the presence of a draining empyema by the escape of retained fluid when forced expiration is performed. In the presence of an empyema cavity or a pneumothorax, the patient is required to execute the forced expiratory exercises as often as every hour during the day. They may not be instituted in the presence of an open bronchial fistula.

Following traumatic lesions of the chest involving lacerations of the lung a prolonged convalescence is indicated. Return to duty should be postponed until roentgenographic evidence of intrapulmonary damage has largely disappeared and is minimal.

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AFFERENT VASODEPRESSOR NERVE IMPULSES AS A CAUSE OF SHOCK: TESTED EXPERIMENTALLY BY AORTIC-DEPRESSOR NERVE STIMULATION*

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ONE of the oldest theories of shock accompanying injury by either accidental or militant violence or by surgery is that it may result from an insult to the nervous system. The most prevalent conception of the mechanism is that excessive afferent depressor nerve impulses are set up either in the wound or in the cerebrum which act upon the vasomotor center, and to a lesser extent upon the cardiac center in the medulla, causing a fall in blood pressure of such magnitude and duration that the circulation becomes inadequate, the tissues are damaged and the bodily functions are impaired. The prolongation of such a state is thought to result in complete circulatory failure and death. The term "primary shock" has been widely used to denote a condition presumably produced in this way. The mechanism has also been considered as a contributing factor where other causes, as hemorrhage, are primary. Most of the members of the medical profession attach some importance to the theory and it is discussed with varying degrees of favor in nearly all textbooks of surgery and physiology. Crile[1] was for many years the chief exponent and the American Red Cross First Aid Book[2] gives this in simpler terms as the mechanism of shock production. Any theory of shock that receives this amount of credence is worthy of careful analysis as to its merits.

Before considering the effects of afferent depressor nerve impulses, it is well to review briefly the more important influences of the nervous system on the blood vessels and heart. Control of the blood vessels is exercised principally through the vasomotor center in the medulla as shown schematically in Figure 1. Efferent impulses pass from it by pathways in the spinal cord to the sympathetic and parasympathetic systems, and in case of vasodilators to a limited extent to the somatic nerves (antidromic fibers), and thence to the vascular system. They are both vasoconstrictor and vasodilator but the former predominate in the lowering of general blood pressure as proven by the fall of blood pressure to shock levels after section of the spinal cord at C-8. Afferent impulses pass to the vasomotor center by way of the somatic and aortic-depressor (or cardio-aortic) and carotid sinus nerves and from the cerebral cortex. Both pressor and depressor afferent impulses

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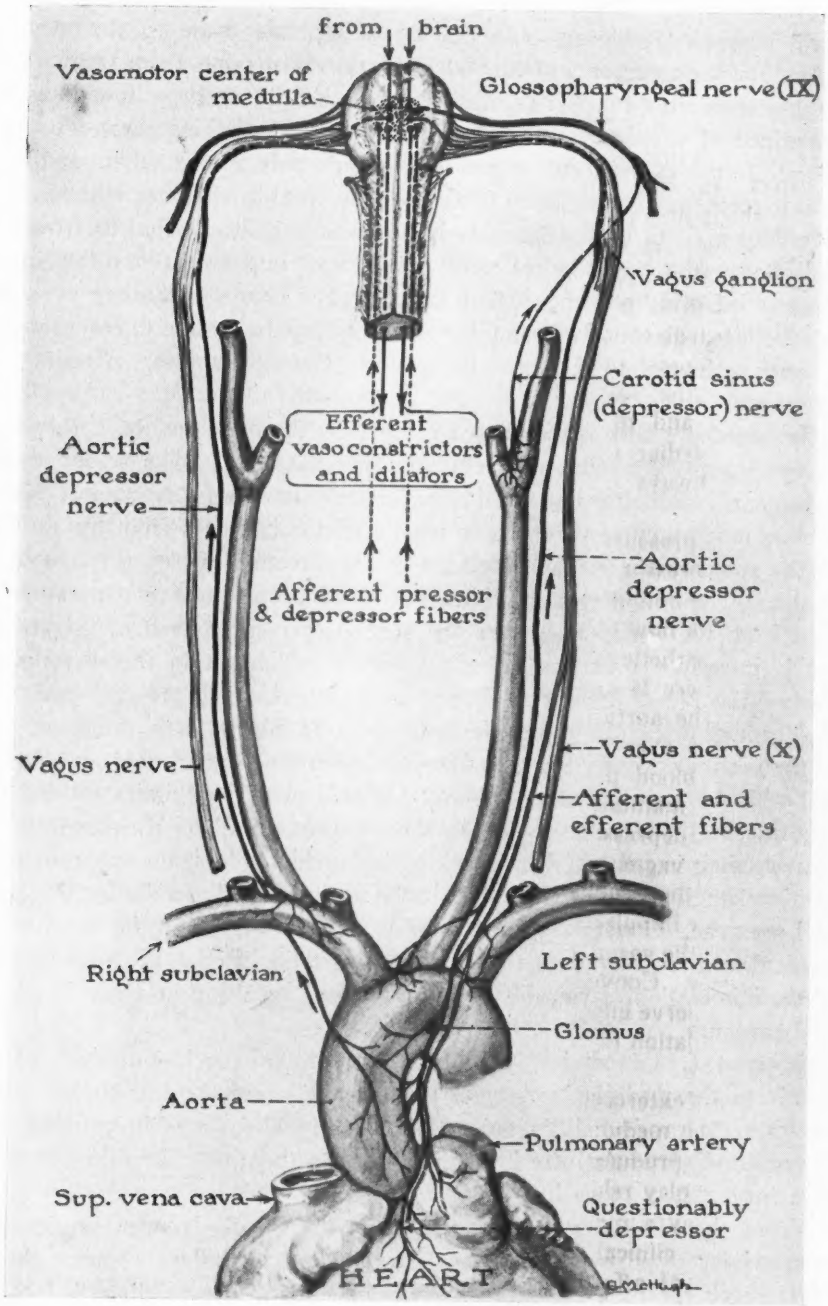


FIG. 1.—Schema of carotid sinus and aortic-depressor nerves and of principal afferent and efferent medullary pathways.

come over the somatic nerves having separate pathways in the spinal cord, as shown by Ranson and Billingsley,[3] and over pathways from the cerebral cortex. However, only depressor impulses come to the medulla over the aortic-depressor and carotid sinus nerves making them particularly favorable structures for isolation and stimulation in an experimental study of the effects of vasodepression from afferent impulses. The aortic-depressor fibers are found as separate nerves in the neck only in the rabbit and in a certain percentage of cats, being fused with the vagi in all other animals.

Nervous control of the heart is by efferent inhibitor impulses from the medulla over the vagi, by efferent accelerator impulses from the upper thoracic cord and to some extent from higher centers, passing over the sympathetic cardiac nerves, and by afferent impulses over fibers in much the same pathways to the medulla as are afferent impulses affecting the blood vessels.

The blood pressure is modulated reflexly by the maintenance of a balance between vasopressor and vasodepressor impulses and to a lesser extent between cardio-inhibitor and cardio-accelerator impulses (Heymans[4]). There is a continuous flow of vasopressor or constrictor impulses from the medulla over the sympathetic nerves which act in the direction of elevating the blood pressure. There is also a continuous flow of proprioceptive depressor impulses from the aortic arch over the aortic-depressor nerves and from the carotid sinuses over the carotid sinus nerves which act in the direction of lowering the blood pressure. Some investigators, as Heymans[4] and Daly and Verney,[5] maintain that afferent depressor fibers from the heart also join the aortic-depressor fibers to form a single nerve in the rabbit or a bundle fused with the vagus in other animals. Within prescribed limits any increase in pressure in the vessels supplied by these nerves stimulates their endings and augments their impulses (Bronk and Stella[6]), which inhibit the vasoconstrictor and stimulate the vasodilator centers in the medulla causing a decline in general blood pressure. Conversely, any decrease in pressure within the same vessels retards these nerve impulses, thereby lessening the inhibition of vasoconstrictor and the stimulation of vasodilator impulses, and resulting in a rise in general blood pressure.

Afferent (exteroceptive) impulses, both pressor and depressor, coming directly to the medulla by way of the somatic nerves appear under normal conditions to produce little more than fleeting alterations in general blood pressure and play relatively little part in its modulation. Impulses from the brain may play a more important rôle.

From the clinical standpoint, if traumatic shock is ever produced by hyperactivity of afferent depressor impulses on medullary centers, the impulses reach the medulla either by way of somatic nerves directly from the injured field or from the cerebrum where they may be set up by distressing special sense perceptions as the sight of blood or of the injured field, or by pain perception. The low blood pressure in syncope is a manifestation of such cerebral activity. The aortic-depressor and carotid sinus (proprioceptive)

nerves, although the most effective vasodepressor nerves, are obviously so small and so situated anatomically that they would never be directly injured and continuously stimulated to produce shock. Sudden reflex death, usually respiratory but possibly also cardiac, sometimes occurred during dissection of the carotid sinuses in dogs when they were being prepared in a set of stimulation experiments but reflex death was never encountered in the aortic-depressor nerve experiments. The cause of the prompt lowering of blood pressure that is sometimes observed during manipulations within the abdomen of man is imperfectly understood. It appears to result from reflex vasodepression and there is associated cardiac inhibition. Whether the afferent impulses travel by way of proprioceptive fibers of abdominal blood vessels that may be contained in the vagi or by way of somatic or sympathetic nerves remains to be clarified.

From the experimental standpoint, the three possible ways of attempting the production of shock by hyperactivity of afferent depressor impulses on centers in the medulla are by stimulation, first, of the trunks or receptors of the somatic nerves; second, of the proprioceptive aortic-depressor and carotid sinus nerves; and third, of the depressor centers of the cerebral cortex. The effects of the lowered blood pressure should be the same by whichever method produced, provided the degree and duration of the lowering and the anesthesia and trauma associated with the experiment were the same.

It appears that no attempt has been made to stimulate the depressor centers of the cerebral cortex with the intention of producing shock, but judging by the results of stimulation reported by Hoff and Green,[7] Schafer,[8] and others, in certain animals, the prospects for success with existing technics are unfavorable since the fall in blood pressure was relatively brief and slight.

By far the simplest and most efficient way of producing marked and prolonged lowering of blood pressure by hyperactivity of afferent vasodepressor impulses is through stimulation of the aortic-depressor (cardioaortic) nerves in rabbits. The results achieved by Phemister and Schachter[9] by stimulation of the carotid sinuses in dogs were similar to but less marked than those to be reported here for the aortic depressor nerves. They are very small structures lying back of the common carotid arteries and just mesial to, and parallel with, the slightly larger cervical sympathetic chains. Their endings are in the arch of the aorta and some authors still claim, in the heart. Several animals were dissected for cardiac fibers in this series and none found.

EXPERIMENTAL METHODS

Because of the unusual sensitiveness of the rabbit to anesthesia, the very small size of the aortic-depressor nerves and the delicacy of the femoral arteries for cannulation, it was found necessary to work only with large animals such as the Flemish Giant breed. With few exceptions, the successful results were obtained with animals weighing from 4 to 6 Kg. The circulating blood volume

derived by the Evans blue dye method on 17 animals averaged 6.8 per cent of the body weight. The average amount of blood obtained (bleeding volume) by bleeding 10 rabbits to death under urethane anesthesia was 48.5 per cent of the calculated blood volume. Average blood analyses in rabbits were as follows: For 100 animals, R. B. C. 6.13; Hb. 80.8; Hcr. 37.5; 50 animals, arterial blood oxygen 6.74 Mm/L and CO_2 17.71 Mm/L; 29 animals, plasma proteins 5.88 Gm. per cent. Blood losses from surgery and cannula clot washings were calculated in most cases with the aid of the Evelyn colorimeter from determinations of hemoglobin removed from the sponges and wash basins.

Anesthesia was produced by urethane administered intraperitoneally. After experience with doses 25 to 100 per cent larger, it was found that the most satisfactory results were obtained with 500 mg. per Kg. body weight. In animals not experimented upon the anesthesia wore off in three to four hours. A small amount of ether was sometimes added during surgery in case the animal was noisy.

The animal was placed on its back on a dog board and the extremities anchored with cords. The front limbs were held against the sides by passing the cords behind the back and over the front of the opposite forelegs before tying them together beneath the board. A heavy ligature was passed around the symphysis of the mandible with a curved needle. The bit of the head piece of the dog board was then passed between the teeth and the mandible was tied firmly to it.

The femoral arteries were then exposed below Poupart's ligament, the branches tied off and cannulae made from No. 16- to 18-gauge needles inserted for obtaining blood samples on one side and for kymographic recording of blood pressure on the other. A blood sample was usually drawn at this time.

The nerves were then isolated through a midline incision from the larynx to the sternum. The carotid sheath was exposed on either side by separation of the overlying neck muscles. With a toothless forceps, the carotid artery was lifted slightly forward and mesialward by an assistant, while the operator displaced the vagus lateralward and backward. This brought into view the two small nerves closely approximated and held loosely together by fibers of the carotid sheath. The mesial trunk, which is usually the smaller, is the aortic-depressor nerve while the lateral is the cervical sympathetic trunk. Beginning below, they were separated and freed with care by use of fine dissecting instruments, after which threads were passed about them for retraction. Despite these precautions, injury was common and many experiments were spoiled in this way. The left aortic-depressor nerve usually appeared to be slightly larger than the right and often gave a greater response on stimulation.

The cannula of one femoral artery was next connected with the kymograph tubing system and the blood pressure recording was begun.

A shield electrode was placed on the trunk that was considered to be the aortic-depressor nerve on either side and each nerve tested for blood pressure response. The Harvard inductoriums were activated by alternating

current received from a six-volt transformer. If the pressure failed to fall on appropriate stimulation, it usually meant either injury to the nerve or that the sympathetic was being stimulated by mistake in which event there was usually a slight rise in pressure.

TYPES OF EXPERIMENTS

The effects produced by stimulation of the aortic-depressor nerves on blood pressure (pulse, respiration, blood cytology, blood chemistry, survival time, and gross and microscopic anatomy have been determined in varying degrees of completeness according to the stage of development of the work and the available facilities. Factors that have sometimes modified the results adversely have been trauma to tissues and blood loss incident to the operation, withdrawal of blood samples, blood loss from cannula washings, the anticoagulant employed and hot weather. Samples consisted of 4.5 cc. of arterial blood when red cell, hemoglobin, hematocrit, plasma proteins, oxygen and carbon dioxide determinations were made and of one cc. when only the first three were made. Sodium citrate which was used as the anticoagulant in the cannula in all rabbits up to No. 98 produced slight toxicity in some cases and there was more blood loss from cannula clotting and washing than occurred with saline and heparin, which was used in all rabbits above this number. Rabbits tolerated the experiments very poorly during the hot days of summer, often developing a low blood pressure and dying relatively early without stimulation, so that all experiments done at that time had to be discarded.

Interference with stimulus has resulted not only from traumatism to the nerves during isolation but also from drying and from leakage of current due to accumulation of fluid in the wound and contact with surrounding muscles. The electrodes were usually brought into the subcutaneous region and the skin clamped about them. At the onset of recording on the kymograph, the blood pressure was found to range between 80 and 120 Mm.Hg, the average for 100 rabbits being 103 Mm. The pulse was then found to be usually above 200 per minute and rarely lower than 160. The respirations ranged between 40 and 80 per minute.

In control experiments the set-up was as described here but no stimulus was applied to the nerves. The results in three cases are shown in Table I. The average survival time was 14.66 hours. The blood pressure was well preserved until relatively late in two experiments and declined more gradually in one. Hemodilution developed in all cases. Figure 2 shows a condensed tracing of blood pressure with the pulse and respiration rates, and Table II the blood findings, of Experiment 78, in which the survival time was 18.5 hours. Blood loss throughout the course of the experiment from repeated cannula washings and sample withdrawals was unusually high, amounting to 26 per cent of the calculated blood volume, but despite this fact, the blood pressure remained above a shock level until one hour before death. Micro-

scopic examination of sections of tissues showed slight acute degenerative changes in the viscera.

TABLE I

CONTROL RABBITS FOR AORTIC-DEPRESSOR NERVE STIMULATION EXPERIMENTS

Exp. No.	Wt. Kg.	Urethrane mg./Kg.	Survival Time	Initial Pressure Mm.Hg.	Pressure Levels and Time Elapsed from Start	Blood Changes: Time	Hcr. %	Hb. Gm.	R.B.C. M.
46	4.4	500	13 hrs.	90	70 to 100 in 4 hrs. 100 to 80 in 8 hrs. 80 to 0 in 1 hr.	Initial	29	10.7	4.98
						Final	20	8.2	3.16
57	4.4	500	12.5 hrs.	80	80 to 50 in 12.5 hrs.	Initial	37	13.6	5.92
						Final	32	12.4	5.30
78	4.7	500	18.5 hrs.	110	110 to 100 in 16 hrs. 100 to 66 in 2 hrs. 66 to 0 in 0.5 hr.	Initial	36	13.1	6.94
						Final	27	8.8	4.60
Average survival.....			14.66 hrs.						

TABLE II

RABBIT NO. 78 (FIG. 2)

Time Hrs.	R.B.C. M.	Hb. Gm.	Hcr. %
0	6.94	11.9	36
2.0	6.80	11.7	36
5.5	5.66	10.4	31
9.0	5.10	9.6	30
13.0	5.58	9.8	31
18.0	4.60	8.1	27

EFFECTS OF STIMULATION

Various effects of lowering the blood pressure to different levels for different but substantial lengths of time by nerve stimulation were studied in a series of 28 rabbits in which the circulation had not been disturbed otherwise than by the set-up of the experiment. A brief account of the findings has been reported by one of us (D. B. Phemister[10]).

Under favorable experimental conditions, the blood pressure was reduced in the course of two or three minutes to low levels and the heart slowed to 60 to 100 beats per minute by stimulation of both nerves with the secondary coils placed 8 to 10 cm. from the primary coils. Under continued stimulation, the pressure might remain low for long periods of time without increase of the strength of the stimulus or it might rise gradually, necessitating periodic increases in strength to keep it down. When one nerve only was stimulated, the blood pressure remained at a higher level than when both were utilized and a stronger stimulus had to be applied to attain a low level. After the initial bradycardia, the pulse rate increased during the next few minutes but usually remained somewhat retarded as long as the stimulus was continued. Removal of the stimulus was followed by a rapid return of blood pressure to the vicinity of the previous level and by acceleration of the pulse rate. Respirations were little influenced directly by the stimulation. In many un-

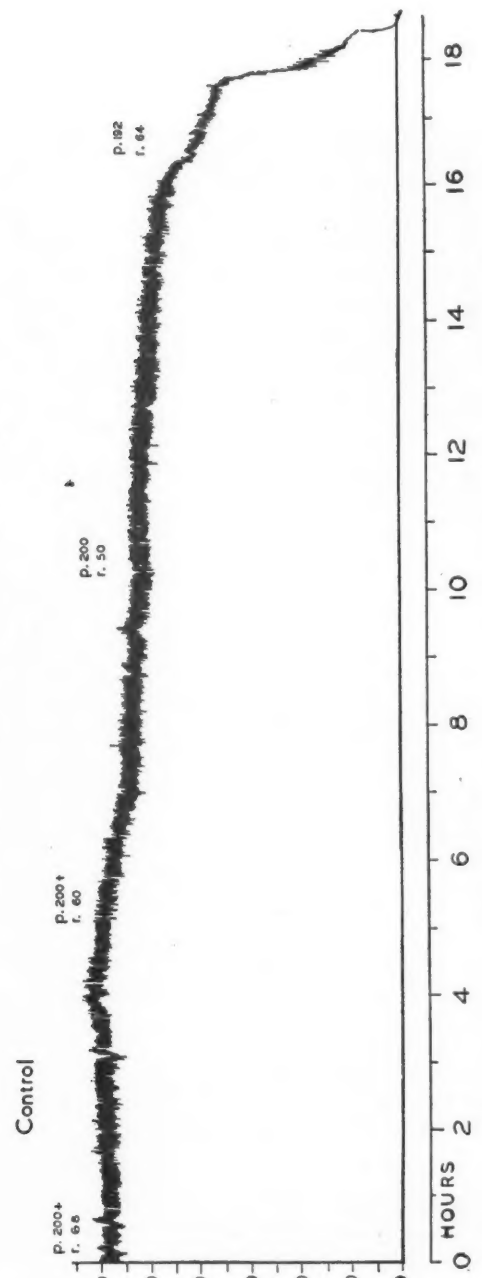


FIG. 2.—Condensed blood pressure tracing and pulse and respiration rates of control for aortic-depressor nerve stimulation experiments.

reported experiments it was impossible to reduce the blood pressure to a shock level or, if so, to hold it at the desired level for the necessary length of time regardless of the strength of the stimulus employed.

Sometimes a relatively weak stimulus produced the maximum vasodepressor effect as shown by the fact that a further increase in strength caused no more decline and in no case was it possible to produce sudden death of the animal by applying the maximum stimuli carried by the two inductoriums. These changes are illustrated in Figure 3, Rabbit 122. At the beginning of the recording the blood pressure was 115 Mm.Hg and the pulse was over 200. With the secondary coil at 9 cm., first the right and then the left cardio-aortic nerves were stimulated, the fall in blood pressure being slightly greater from the left than from the right nerve. After a four-minute rest period, both nerves were stimulated and the blood pressure fell from 105 to 25 Mm.Hg in 1.5 minutes, during which time the pulse dropped to about 60 beats per minute. The pressure then rose to 40 Mm. during the next minute and the pulse increased to 96 per minute. The pressure soon declined to the vicinity of 30 Mm.Hg where it remained for the rest of the half-hour period of continuous stimulation. The stimulus was then released for ten minutes, whereupon the blood pressure quickly returned to the vicinity of the previous level and the pulse increased to 180 per minute. Since the blood pressure was so rapidly reduced and maintained at such a low level by stimulation, with both secondary coils at nine cm., it was thought that using the maximum current from the inductoriums, obtained by placing the secondary coils at the zero points, might cause either further lowering of pressure or death of the animal. However, when this was done, the blood pressure dropped quickly to the vicinity of the previous level, after which it slowly rose. The pulse was retarded, being 128 per minute after four minutes and 140 after 22 minutes, and the animal survived six hours of stimulation with short periods of interruption as will be reported later (Fig. 11).

CONTINUOUS STIMULATION

In other experiments, the blood pressure would remain at higher levels but within the range which is encountered in well marked shock as produced by straight bleeding or by limb trauma. In the majority of cases of effective stimulation, the pressure could be kept at low levels for several hours during which period release of the stimulus would be followed by a prompt restoration of the pressure to, or slightly under, previous levels and by rapid recovery of the circulation. Reapplication of the stimulus would cause an immediate decline which for a few minutes usually went slightly lower than the previous depression. If stimulation continued to be effective, the blood pressure eventually tended to drift to a lower level and the pressor response on release gradually weakened until it became very slight or was exhausted and the animal died. Respirations were usually shallow toward the end. The survival period of six such animals under continuous stimulation, except

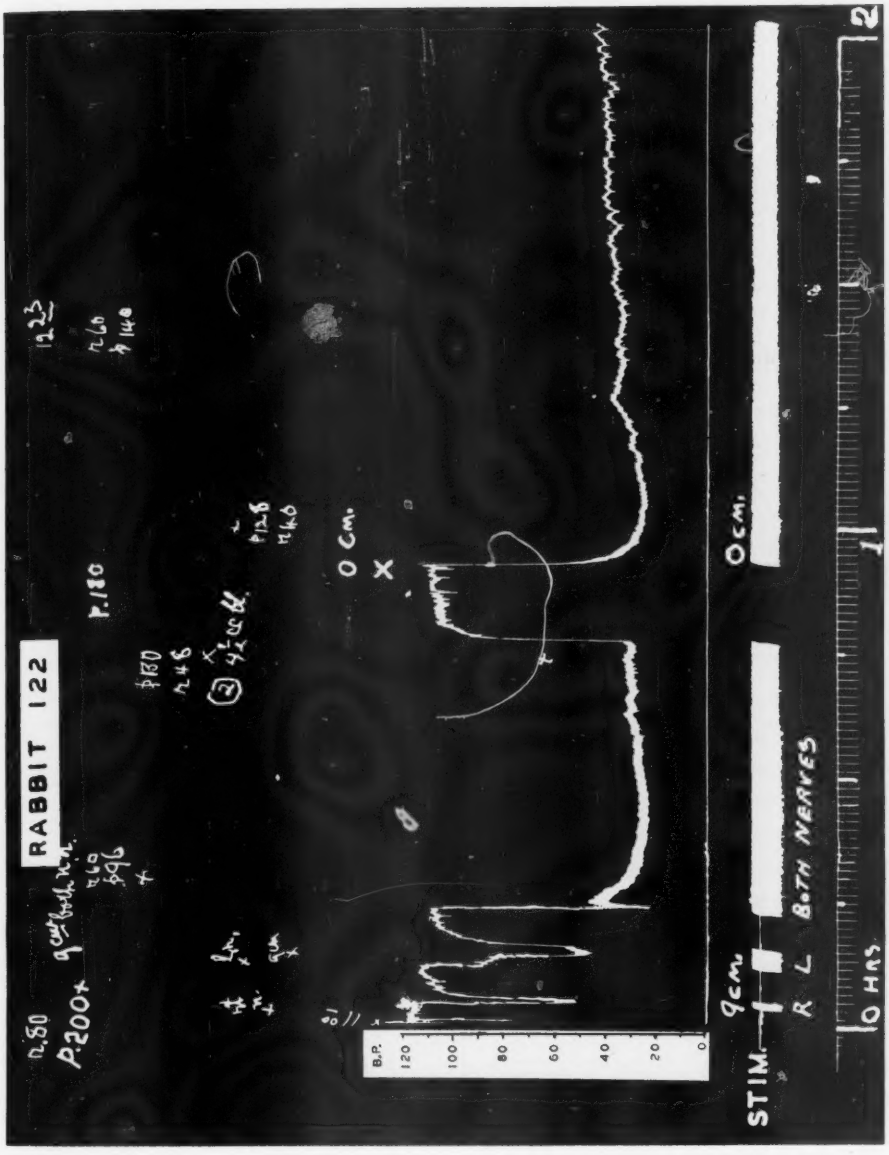


FIG. 3.—Showing comparison of vasodepressor effects from a relatively weak and a very strong stimulus applied to the aortic-depressor nerves of a rabbit.

for the short test releases, varied from 2.5 to 13 hours for all ranges of shock level, averaging 6.75 hours. In general, there was a direct relationship between the level of the pressure and the length of survival, the lower the pressure and the smaller the pulse pressure, the shorter the survival time.

Figure 4, Rabbit 147, shows a condensed tracing of the shortest and most rapidly fatal experiment. At the beginning there was a low irregular pressure following stimulation of the right nerve with the secondary coil at

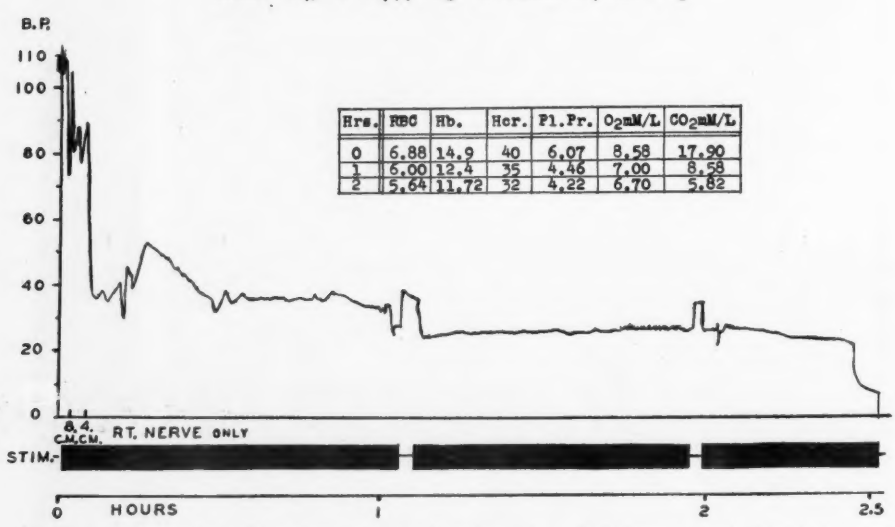


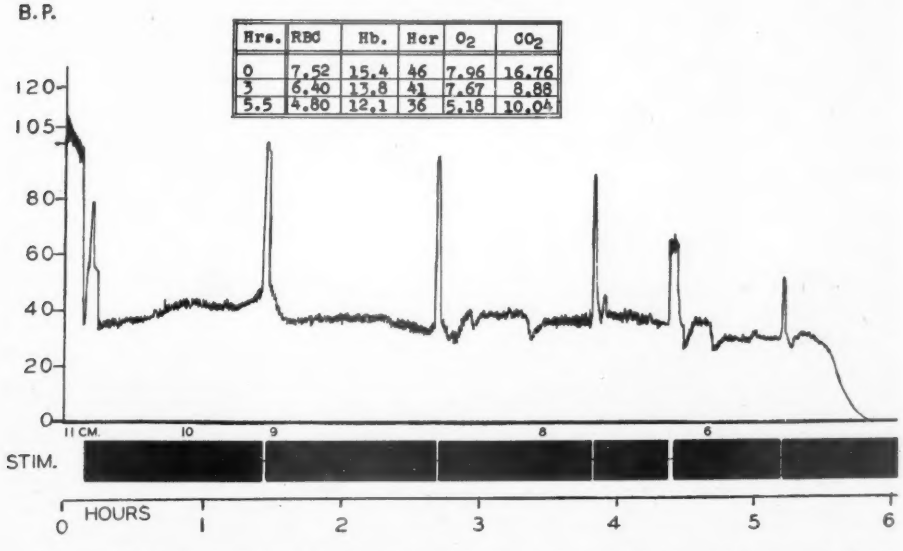
FIG. 4.—Changes in blood pressure and blood produced by aortic-depressor nerve stimulation; early loss of vasoconstrictor tone and early death.

four cm. The pressure then steadily declined to 28 Mm.Hg at the time of death 2.5 hours later. Release of the stimulus just beyond one hour and just short of two hours of the onset of stimulation showed very feeble rises of blood pressure. The blood loss was 14 cc. from cannula wash and hemorrhage and 15 cc. from samples, totaling 8.9 per cent of the estimated blood volume which was a factor of little importance in the causation of death. The blood analyses showed a steady severe reduction in red cells, hemoglobin, hematocrit, plasma proteins, oxygen and carbon dioxide of the arterial blood. The blood changes and the failure of the vasopressor center appeared to be the cause of the rapid death. Necropsy revealed no significant gross changes. Microscopic examination revealed moderate congestion of the lungs and kidneys and marked congestion with sinus dilatation of the spleen. Liver, adrenal, pancreas, heart and striated muscle showed no changes.

Figure 5, Rabbit 75, shows the more usual course where the blood pressure, except for a short rise after the initial fall due to leakage of current, stayed slightly under 40 Mm.Hg for four hours, with each short release resulting in a prompt elevation to approximately the original level, indicating that the circulatory mechanism was still intact. Under continued stimulation the

pressure declined slowly and the pressor responses on release weakened rapidly until the animal died at the end of 5.5 hours. The stimulus was increased from 11 cm. to eight cm. during the first 5.5 hours and to six cm. for the remaining period. Again the blood showed a steady reduction of red cells, hemoglobin, hematocrit oxygen and carbon dioxide, except for an increase in the last carbon dioxide determination.

Rabbit 75 Wt. 4.55 Kg. Urethane 2.28 Gm. i. p.



Hrs.	RBC	Hb.	Her	O_2	CO_2
0	7.52	15.4	46	7.96	16.76
3	6.40	13.8	41	7.67	8.88
5.5	4.80	12.1	36	5.18	10.04

FIG. 5.—Blood pressure tracing showing vasodepression from aortic-depressor nerve stimulation with progressive increase in stimulus strength, gradual loss of vasoconstrictor tone and hemodilution.

Necropsy showed little gross evidence of change. Microscopic examination of pancreas, adrenal, heart and skeletal muscle revealed normal findings. The liver and lungs were moderately congested and the spleen markedly so. The liver showed acute focal necrosis. Scattered cells and clusters up to 25 cells revealed cell fragmentation and disintegration of nuclei (Fig. 6). There were large lymph spaces in the folds of the duodenal lining.

Figure 7, Rabbit 54, illustrates a case in which the blood pressure remained around the relatively high level of 60 Mm.Hg during the first three hours of stimulation with a weak current (nine to 11.5 cm.). Response of pressure to release of the stimulus on two occasions was marked. After increasing the strength of the stimulus to 8.5 cm., the pressure declined gradually and the responses on release weakened for the next two hours. Then with the pressure at 40 Mm.Hg, a rapid decline set in as if death were imminent, for which reason the stimulus was removed. The circulatory mechanism was so nearly exhausted that the pressure remained at or about 25 Mm.Hg for five minutes before it gradually rose to 35 Mm. When the stimulus was re-applied at the end of 25 minutes there was a very slight depressor response. From then on to 6.25 hours, there was a steady decline of pressure with

no pressor response on two releases of the stimulus. The secondary coil was then moved to 11 cm. and when the weakened stimulus was temporarily released at 6.5 hours, the pressure almost doubled in height, showing improvement in the vasoconstrictor mechanism. Renewal of stimulation was followed by a fall to the previous level and then by a steady decline until death at seven hours. Red cells showed a progressive dilution from the control count

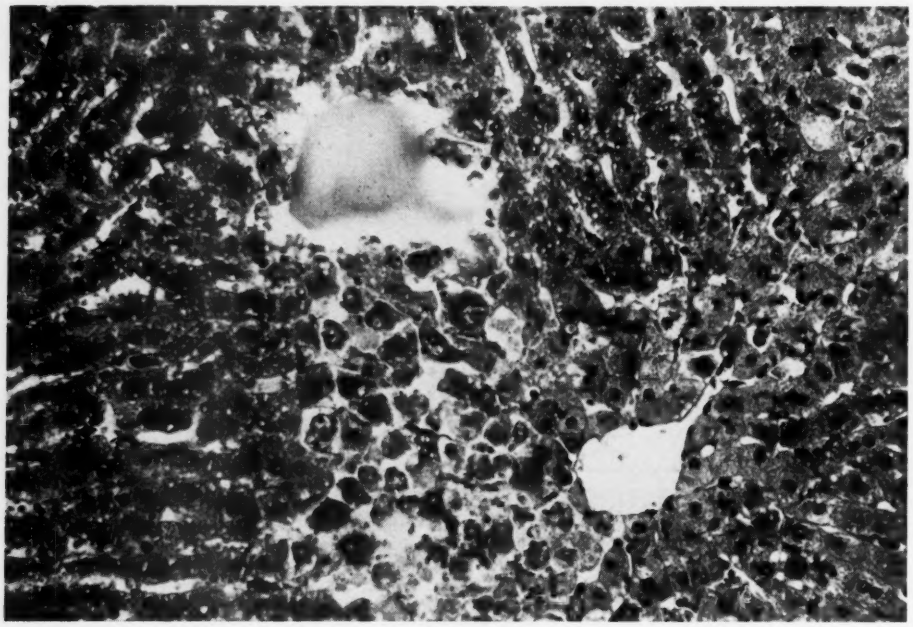


FIG. 6.—Rabbit 75: Focal necrosis of liver and lymph accumulation in necrotic area. (× 300)

of 7.04 to 6.24 at six hours, with terminal concentration to 6.70 on a sample taken 20 minutes before death.

Necropsy revealed gross congestion of the spleen and hypostatic congestion of the lungs. Microscopically, there was acute focal necrosis of the liver, protein precipitation in a few of the pulmonary alveoli and congestion of a dorsal section of lung. A section of jejunum showed marked lymphatic distention and lymphorrhexis into the subserosal and submucosal spaces. There was no evidence of acute changes in sections of other tissues.

Two other experiments gave similar findings and are not reported in detail. Rabbit 27 lived for four hours and Rabbit 91 for seven hours and 30 minutes from the onset of stimulation. The bladders of all animals contained but a small quantity of urine, rarely more than ten cc. in all of the five experiments just reported, indicating suppression of secretion with the low blood pressure.

Figure 8, Rabbit 52, is a remarkable illustration of the relatively harmless effect of neurogenic lowering of the blood pressure in the upper range of what is arbitrarily designed as the shock level, *i.e.*, 70 Mm.Hg or below. On stimulation, the pressure dropped from 90 to between 50 and 60 Mm.Hg in

which vicinity it vacillated for five hours. The stimuli were relatively weak, eight to ten cm., and four releases during the period resulted in good pressor responses, the last one being somewhat reduced. At five hours the secondary coil was moved to seven cm., but the pressure slowly rose, reading 70 Mm. at 6.5 hours. The coil was then moved to five cm. and the stimulus maintained the pressure in the vicinity of 65 Mm.Hg for the succeeding 2.75 hours. Because of a gradual rise of pressure, the coil was then moved to four cm. After a slight drop, which was sustained for 30 minutes, the stimulus was weakened by current leakage to the tissues and the pressure went up to 80 Mm. within

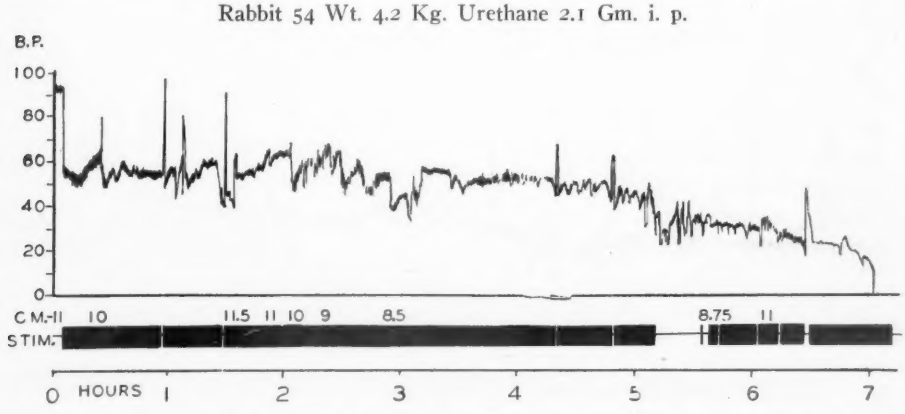


FIG. 7.—Prolonged vasodepression from aortic-depressor nerve stimulation with progressive loss of vasoconstrictor tone and death. Weak stimulus in early period.

30 minutes. On release of the stimulus at 10.33 hours for six minutes, the pressure rose to the initial level. Renewed stimulation gradually lowered the pressure to 45 Mm.Hg at 12 hours when another release resulted in a pressor response to 90 Mm.Hg. The pressure then fluctuated and was at 50 Mm.Hg 13 hours from the onset when death occurred suddenly, preceded by a momentary pressor response of 20 Mm. on removal of the stimulus.

Eight red cell counts over the course of 11.75 hours showed a gradual decline to 5.12 from the control of 7.12. Hemoglobin and hematocrit readings had to be discarded because of faulty technic. Necropsy revealed gross evidence of congestion of spleen and kidneys and a light-colored liver. Microscopically, there was marked focal degeneration and necrosis of cell groups and scattered single cells in the liver. The lungs showed some dilated lymph channels and tiny hemorrhages. The kidneys had been eliminating red blood cells as indicated by their presence in the tubules of the papilla. Blood vessels were moderately congested. There was a little degeneration and sloughing of epithelium in the cortical tubules. The jejunum contained a few dilated lymph channels and there were many distorted nuclei and lymphocytes in the mucosa. Changes in other organs and tissues were insignificant.

The significance of the findings in this group of experiments is considered in the general discussion after the results of other relevant experiments have been given.

STIMULATION AND RELEASE

Figure 9, Rabbit 79, illustrates the ability of an animal to recover from the effects of prolonged lowering of blood pressure after removal of the stimulus either permanently or for a long period of time. During a four-hour period of stimulation, with a current that was progressively strengthened by moving the secondary coil from ten cm. to five cm. the blood pressure was maintained at levels fluctuating between 30 and 60 Mm., with an average pressure in the vicinity of 50 Mm. During this period the blood showed a fluctuating tendency to dilution and five brief releases of stimulus yielded

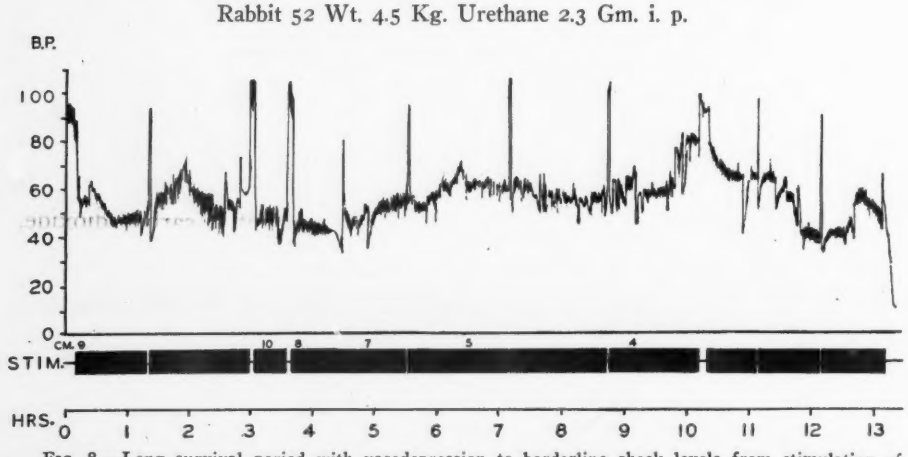


FIG. 8.—Long survival period with vasodepression to borderline shock levels from stimulation of the aortic-depressor nerves with little impairment of vasoconstrictor tone to within one hour of death.

well marked pressor responses. After 3.75 hours stimulation was discontinued, whereupon the blood pressure rose in less than a minute to the level before stimulation. It continued to remain in that vicinity for hours and was at 90 Mm.Hg when the animal was killed seven hours after discontinuing stimulation. The blood was considerably diluted after two hours but was less so after 3.75 hours. Three and three-quarters hours after stopping the stimulus there was concentration slightly above that of the initial sample.

Animals which had long periods of vasodepressor and eventual weakening or exhaustion of the stimulus showed the same tendency to recovery and long survival.

The influence of blood and plasma on an animal whose circulation had been impaired by prolonged lowering of blood pressure by aortic depressor nerve stimulation was tested in seven rabbits, five by blood transfusion and two by plasma transfusion.

Figure 10, Rabbit 133, shows a condensed tracing of a severe vasodepression resulting from a relatively weak stimulus. The blood pressure declined promptly from 105 Mm.Hg to 40 Mm., returning to the original level during a one-minute release period at the end of 30 minutes. Subsequently the pressure declined gradually to 22 Mm. at the end of three hours

and the animal appeared to be near death. The stimuus was then removed for five minutes, during which time the pressure responded very feebly, rising to 36 Mm.Hg. Examination of blood samples (Table No. III) taken before

TABLE III

RABBIT NO. 133 (FIG. 10)

Sample No.	Time Hrs.	R.B.C. M.	Hb. Gm.	Hcr. %	CO_2 Mm/L	O_2 Mm/L	Plasma Proteins Gm.%
1	Control	6.56	14.0	42.5	15.80	8.34	6.56
2	1.0	6.68	14.6	43.5	11.58	8.14	6.00
3	3.25	6.50	13.5	41.5	9.24	8.14	5.95
	3.25	Transfused 72 cc. Blood (20% of estimated blood volume)					
4	4.33	7.60	15.4	47.0	10.58	9.29	6.82
5	8.33	8.30	16.2	54.0	.....	....	7.72
6	10.5	7.44	15.4	47.5	.....	....	7.66

the onset of stimulation, one hour after and again 2.1 hours later, at the end of a five-minute period of release of the stimulus, revealed practically no changes in red cell counts, hemoglobin, hematocrit and oxygen, but a reduction of 9 per cent in plasma proteins and 31 per cent in carbon dioxide.

Rabbit 79 Wt. 5.7 Kg. Urethane 2.85 Gm.

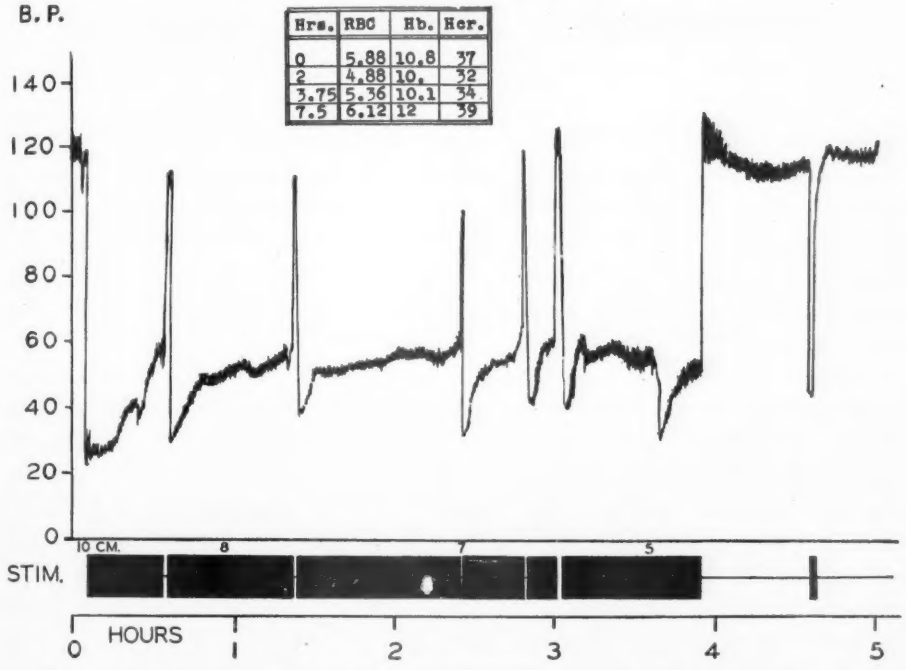


FIG. 9.—Vasodepression from prolonged aortic-depressor nerve stimulation showing maintained vasoconstrictor tone and capacity of circulation to recover after release of stimulus.

These relatively slight blood changes indicate that it was not oxygen deficiency but marked damage to the vasodepressor center, as shown by the feeble pressor response on release of stimulus that caused the severe embarrassment of the circulation.

When the stimulus was reapplied, the blood pressure declined rapidly to 20 Mm.Hg at which time a transfusion into the opposite femoral artery of 36 cc. of heparinized rabbit's blood was given. The pressure rose during the transfusion and then started down, whereupon the stimulus was released and a second transfusion of the same amount was given. This produced a marked rise followed by a slight fall after which the pressure gradually improved and registered 70 Mm.Hg 4.33 hours after the beginning of

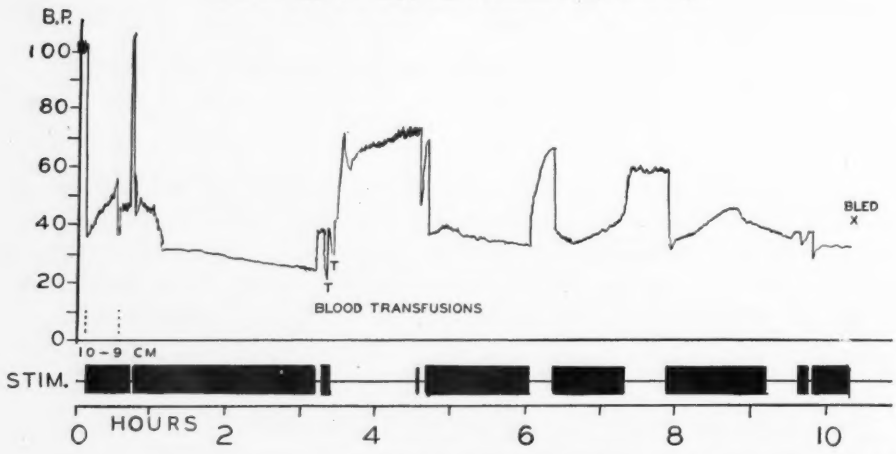


FIG. 10.—Showing improved vasoconstrictor tone and prolonged life from blood transfusion given after a period of marked vasodepression and imminent death from aortic-depressor nerve stimulation.

stimulation. The blood was concentrated after the transfusion. The animal survived long periods of stimulation and vasodepression separated by shorter periods of release and elevation, until the pressor response was almost exhausted at 9.66 hours. There was also much blood lost from clotting and cannula washings causing terminal dilution. Bleeding of 48 cc. at 10.5 hours caused death.

Figure 11, Rabbitt 122, shows a condensed tracing of blood pressure held for 6.75 hours at an average level of about 40 Mm.Hg by stimulation during which there were releases for periods varying from two minutes to ten minutes and totalling 33 minutes. The secondary coil was at ten cm. for the first half-hour and at 0 cm. thereafter. The rest periods, which were relatively long when compared with those in most of the experiments, helped to maintain the vasomotor center in good condition (as shown by the high pressor responses on stimulus release) and to prevent more than slight reduction in the blood elements analysed, as shown in Table IV. The pressure rose almost to the initial level on release of the stimulus at seven hours, the latter becoming ineffective because of leakage of current from fluid accumulation in the wound. At the end of an hour, with the restored pressure remaining constant, a 41 cc. blood transfusion (15 per cent of the estimated blood volume) was given without producing a change in pressure level. After drying out the neck wound, the stimulus was reapplied at nine

hours and the pressure fell again to a low level. After 9.5 hours the animal was bled with the stimulus on and 122 cc. or 45 per cent of the estimated volume of blood was obtained. Twenty-three and one-half cubic centimeters of blood had been removed in samples and cannula washings, making a total of blood loss of 145.5 cc. Despite the fact that the animal had been subjected to prolonged periods of low blood pressure, the circulation was so well preserved at the time the blood transfusion was given that no change in pressure was produced but the bleeding volume obtained subsequently under stimulation was undoubtedly greater than would have been the case without transfusion.

TABLE IV

RABBIT NO. 122 (FIG. 11)

Sample No.	Time Hrs.	R.B.C. M.	Hb. Gm.	Hcr. %	CO_2 Mm/L	O_2 Mm/L	Plasma Proteins Gm.%
1	0	6.18	11.8	36.5	23.00	6.81	6.63
2	0.25	5.58	10.9	33.0	20.59	6.31	5.93
3	2.75	5.80	11.5	34.0	14.79	6.58	5.24
4	4.25	5.40	11.1	32.0	12.75	6.42	5.88
5	6.8	5.40	11.1	32.0	.....	....	....

Fig. 12, Rabbit 124, shows a prolonged period of vasodepression from nerve stimulation with the secondary coil at 6 cm. During this period the circulating blood volume was determined, blood transfusions and adrenalin were given, periodic blood analyses were made and a terminal bleeding volume was obtained. In the course of the first four hours of stimulation with the blood pressure averaging 35 to 40 Mm.Hg, there were variable reductions in the red cells, hemoglobin, hematocrit, plasma proteins, blood oxygen and carbon dioxide. Release of the stimulus for 1.5 minutes at 2.66 hours revealed a moderate reduction in the pressor response but the response was somewhat greater at four hours, probably due to the slightly elevated pressure during the preceding 45 minutes. Forty-five cubic centimeters of blood was transfused at 4.75 hours and 30 cc. at five hours, making a total of 21 per cent of the estimated blood volume. Release of the stimulus after the first transfusion showed additional improvement in the pressor responses. Four minims of 1/15,000 adrenalin solution then produced a marked elevation in pressure which fell to the previous level in three minutes. The blood pressure gradually crept up to 60 Mm. at six hours. Release then produced a marked pressure rise but the response to stimulation became irregular and after 7.4 hours was exhausted, at which time the stimulus was removed and the pressure leveled at 120 Mm.Hg. After eight hours the animal was sacrificed by bleeding 195 cc., or 55 per cent of the estimated blood volume. All of the organs were pale and, microscopically, the liver and kidney showed scattered areas of acute parenchymatous degeneration. This is another example of a very marked vasodepression which was well tolerated for four hours and of improvement of the circulation during effective stimulation by the transfusion of blood.

The blood volume determination was one of a series of five made by Dr. Paul W. Schafer on rabbits during vasodepression to a shock level which had been maintained for two to three hours before beginning the test (Table V). A control sample was drawn, dye was injected and four successive four cc. samples were drawn at ten-minute intervals. A transfusion equal to the total amount of blood withdrawn was given at the end.

Figure 13, Rabbit 139, shows the blood pressure during aortic-depressor nerve stimulation held at a fluctuating but remarkably low level, averaging less than 30 Mm.Hg for four hours, except for the five release periods, totaling

Rabbit 122 Wt. 4 Kg. Urethane 2 Gm. i. p.

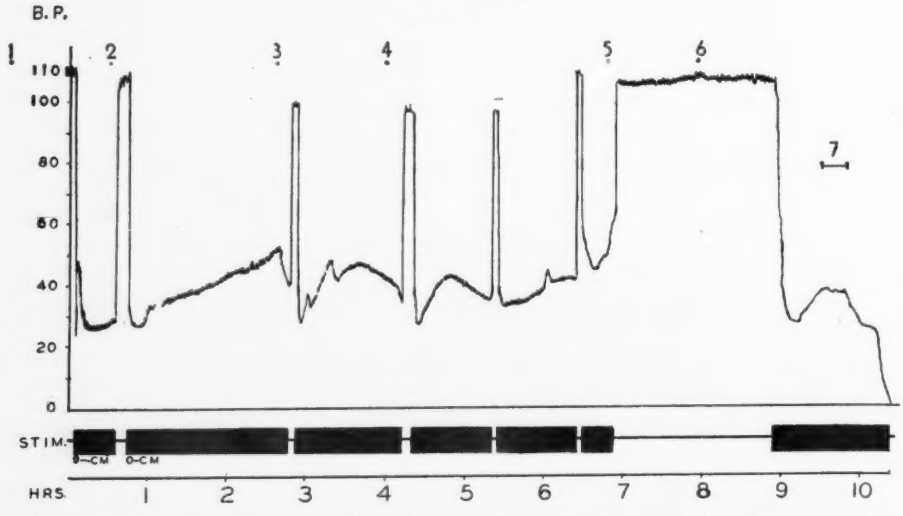


FIG. 11.—Seven-hour period of vasodepression from depressor nerve stimulation, with preservation of vasoconstrictor tone throughout and recovery of blood pressure to normal level during prolonged release of stimulus. Transfusion (6) did not elevate pressure but increased the terminal bleeding volume (7). Blood samples (1) to (5).

ten minutes. The stimulus was started with the secondary coil at ten cm., which was moved to eight cm. at three hours. Release of the stimulus just after one hour and at 2.6 hours showed good pressor responses, but three releases between 2.9 and 3.6 hours showed reductions to the vicinity of two-thirds the original level. The blood constituents determined during this four-hour period showed a gradual decrease with the exception of the red blood cells, hemoglobin and hematocrit of the third sample at 2.25 hours. Both the vasomotor center and the composition of the blood were remarkably well preserved considering the low level of blood pressure during the period.

A plasma transfusion was then given in the opposite femoral artery during which time the pressure recording was stopped. With resumption of the recording, the pressure was found elevated but it quickly returned to the vicinity of the previous level. Release of the stimulus for seven minutes after a 30-minute interval resulted in an elevation of pressure to 100 Mm.Hg with a prompt return to a low level on restimulation. A second transfusion of the same amount produced marked elevation of blood pressure which

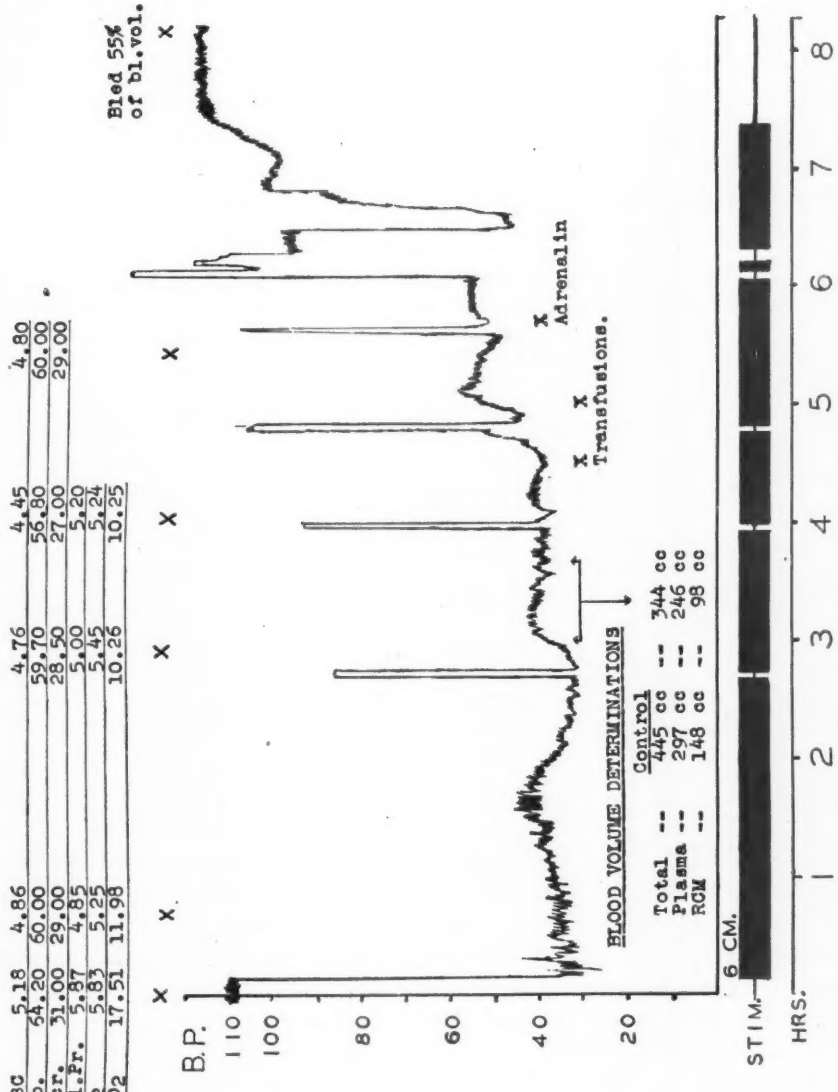


FIG. 12.—Marked lowering of blood pressure well tolerated for four hours. Blood volume estimated toward end of that period moderately reduced. Blood pressure and release responses improved following blood transfusions.

declined to the previous level in 10 minutes. At 5.6 hours, with the stimulus on, the animal was bled 108 cc., or 40 per cent of the estimated blood volume. This lowered the blood pressure to 20 Mm.Hg. On release of the stimulus the blood pressure promptly rose to 60 Mm. showing marked activity of the vasomotor center after severe blood loss. With the pressure again at 20 Mm. from renewal of stimulation, an additional 28 cc., or 10 per cent of the estimated blood volume, was removed before death occurred. Blood analyses after the first and second transfusions at 4.5 and 5.3 hours, respectively, revealed a dilution of the cellular elements, an increase in the plasma proteins, no change in blood carbon dioxide, and first a decline and then a rise in blood oxygen. After the first bleeding there was a further reduction of red cells, hemoglobin and hematocrit.

TABLE V

CIRCULATING BLOOD VOLUME DETERMINATIONS BY THE EVANS BLUE DYE METHOD ON RABBITS IN WHICH THE BLOOD PRESSURE WAS MAINTAINED AT SHOCK LEVEL BY AORTIC-DEPRESSOR NERVE STIMULATION

	Rabbit No. 102	Rabbit No. 119	Rabbit No. 124	Rabbit No. 127	Rabbit No. 130	Average Decrease
Weight	5.1 Kg.	6.0 Kg.	5.2 Kg.	4.7 Kg.	5.0 Kg.	
Elapsed time from start of stimulus	2.5 hrs.	2.5 hrs.	3.0 hrs.	2.0 hrs.	2.25 hrs.	
Control total volume	320 cc.	350 cc.	445 cc.	290 cc.	254 cc.	
Total vol. during stim	304 cc.	275 cc.	344 cc.	248 cc.	204 cc.	
Decrease	16 cc.	75 cc.	101 cc.	42 cc.	50 cc.	
% Decrease	5%	21%	23%	15%	20%	17%
Control plasma volume	203 cc.	200 cc.	297 cc.	185 cc.	168 cc.	
Plasma vol. during stim	214 cc.	175 cc.	246 cc.	173 cc.	161 cc.	
Decrease (Inc.)	11 cc.	25 cc.	51 cc.	12 cc.	7 cc.	
% Decrease (Inc.)	6%	13%	17%	7%	4%	7%
Control red cell mass	117 cc.	150 cc.	148 cc.	105 cc.	86 cc.	
Red cell mass during stim	90 cc.	100 cc.	98 cc.	75 cc.	43 cc.	
Decrease	27 cc.	50 cc.	50 cc.	30 cc.	43 cc.	
% Decrease	23%	33%	34%	29%	50%	34%

The plasma transfusions, while diluting the cellular elements, increased the plasma proteins which had been considerably reduced during the previous period of low blood pressure. The blood oxygen and carbon dioxide were relatively little changed and the vasomotor center was apparently strengthened, as judged by the excellence of the pressure responses on release of the stimulus after the first transfusion and after the first bleeding, which was massive.

In a second experiment, where stimulation maintained the pressure between 40 and 50 Mm.Hg for 2.7 hours and the pressor response on release of the stimulus was to the prestimulation level, the giving of 23 cc. of plasma, or 8.5 per cent of the estimated blood volume, was followed by an increase of 15 Mm. in the height of the response on release of stimulus after 15 minutes. A second similar transfusion after an additional 1.4 hours of vasodepression was followed by a slightly higher pressor response. Bleeding to death then yielded 63 per cent of the animal's estimated blood volume.

Rabbit 139 Wt. 4 Kg. Urethane 2 Gm. i. p.

Hrs.	RBC	Hb.	Hcr.	Pl.Pr.	O_2mM/L	CO_2mM/L
0.	5.28	65.	29.5	5.24	5.88	23.
1.1	4.12	52.	23.5	4.33	5.16	17.17
2.25	5.54	55.	25.	4.19	5.04	16.73
3.7	4.24	51.	23.5	3.79	5.08	13.90
4.5	3.70	45.	21.	4.22	4.30	14.32
5.3	3.38	40.	19.	4.59	4.98	13.53
5.7	2.74	34.	15.	--	--	--

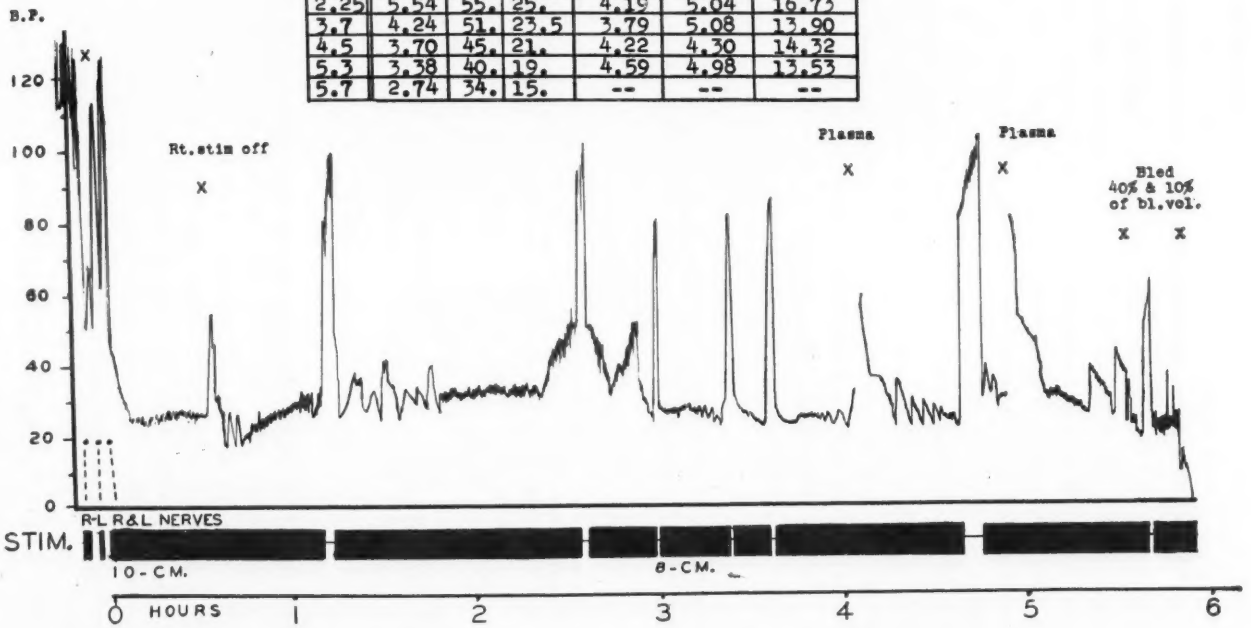


FIG. 13.—Very low blood pressure from nerve stimulation with only moderate blood dilution and reduction of vasopressor response on periodic release during first four hours. Plasma transfusions beneficial.

The results of these experiments warrant the conclusion that when the circulation has been impaired from lowering the blood pressure by the action of vasodepressor nerve impulses, blood or plasma transfusion is beneficial.

HEMORRHAGE AND DEPRESSOR NERVE STIMULATION

In case of accidental wounds in man both hemorrhage and vasodepression from afferent nerve impulses as produced by psychic influences may be active in the lowering of blood pressure and the question arises as to the rôle which each may play in the production of shock. They may occur simultaneously or either one may precede the other. Thus there may be an immediate and marked fall of blood pressure produced by fainting and a subsequent fall of pressure produced by hemorrhage, or *vice versa.*

In testing the relative importance of vasodepressor nerve impulses and hemorrhage in the production of shock, the blood pressure in one group was first lowered by aortic-depressor nerve stimulation and then the rabbits were bled. In a second group the animals were first bled to shock levels and then the aortic-depressor nerves stimulated.

TABLE VI

EXTENT TO WHICH ANIMALS WITHSTAND INTERMITTENT BLEEDING AND CONTINUOUS STIMULATION AFTER VARYING PERIODS OF LOW BLOOD PRESSURE PRODUCED BY AORTIC-DEPRESSOR NERVE STIMULATION

					Duration of Stimulus			% Blood Volume Lost		
Exp. No.	Wt. Kg.	Initial Pressure Mm. Hg.	Stimulus Strength	Pressure During Stimulation	Total Hrs.	Before Bleeding Hrs.	Intermittent Bleeding Time Hrs.	From Bleeding	Samples, Clot, Wash and Surgery	Total
97	3.9	115	9–8 cm.	50–60	1.9	1.0	0.9	45	2	47
84	5.4	110	11–8 cm.	30–60	2.7	1.2	1.5	27	7	34
99	4.0	110	10–9½ cm.	38–46	2.0	1.3	0.7	51	7	58
80	4.9	105	11–9 cm.	20–60	3.2	2.2	1.0	35	9	44
88	4.1	120	10–1 cm.	50–70	3.5	2.5	1.0	26	10	36
82	4.9	110	8–6 cm.	30–60	6.7	4.5	2.2	36	14	50
Averages						2.2	1.2	36.7%	8.1%	44.8

The effect of hemorrhage superimposed on a period of low blood pressure produced by aortic-depressor nerve stimulation was studied in 11 rabbits, six by intermittent bleeding and five by continuous bleeding. Table VI shows that intermittent bleeding after 1- to 4.5-hour periods of vasodepression to definite but not to extreme shock levels was well tolerated, as judged by the amounts it was necessary to bleed for the production of death. They ranged from 36 to 58 per cent of the estimated blood volume and averaged in the vicinity of normal.

Figure 14, Rabbit 82, shows the result in the case of the longest period of vasodepression before intermittent bleeding. The blood pressure averaged about 40 Mm.Hg during the first 4.33 hours, with a gradual rise in the last hour. Table VII reveals a well marked blood dilution and reduction in oxygen and carbon dioxide. The pressor responses during brief releases of the stimulus were well preserved. The animal was bled 62 cc. at 4.33

hours (A), 30 cc. at 5.25 hours (B), 19 cc. at 6.16 hours (C) and 5 cc. to death at 6.5 hours (D)—a total of 116 cc., equal to 36.1 per cent of the estimated blood volume. Including cannula washings and samples, a total of 162 cc., or 50.5 per cent of the estimated blood volume, was lost. Samples of bloods (B) and (C) showed a progressive dilution. Four pressor responses on release of stimulus during the bleeding period showed only moderate reduction but a fifth release just before death gave no response.

TABLE VII

RABBIT NO. 82 (FIG. 14)

Time Hrs.	R.B.C. M.	Hb. Gm.	Hcr. %	CO_2 Mm/L	O_2 Mm/L
Control	5.66	12.0	36.0	18.98	6.98
1.0	4.86	10.5	33.0	15.99	6.32
2.0	4.84	10.5	32.5	....:	....
3.0	4.32	10.1	31.5	13.32	6.41
4.0	4.24	9.3	30.0	8.36*	3.63*
4.33	Bled 62 cc. (19.3% of estimated blood volume)				
5.25	3.38	7.3	21.0	9.11	4.07
5.25	Bled 30 cc. (9.3% of estimated blood volume)				
6.16	2.90	6.6	19.0	6.16	3.85
6.16	Bled 24 cc. (7.5%) to death				

*Micro sample used.

Rabbit 82 Wt. 4.75 Kg. Urethane 2.38 Gm. i. p.

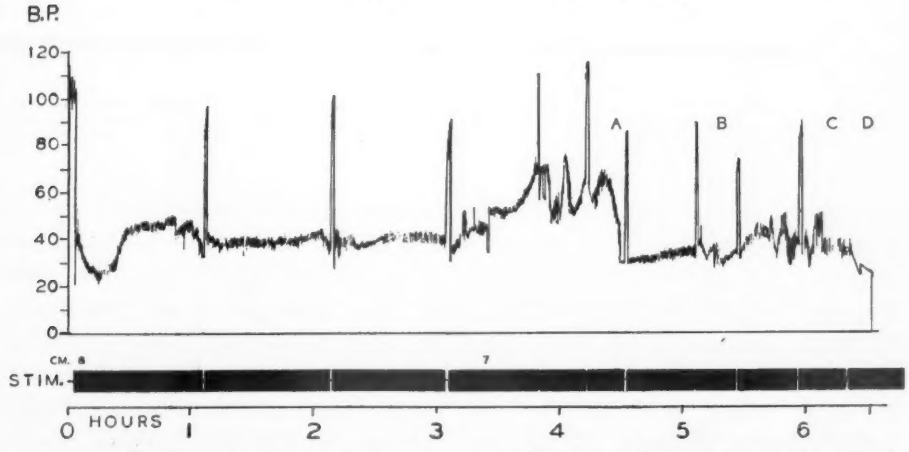


FIG. 14.—Vasodepression from aortic-depressor nerve stimulation with intermittent terminal bleeding well tolerated. Bled A—62 cc. (19.3%); B—30 cc. (9.3%); C—19 cc. (5.9%); D—5 cc. (1.6%); total 116 cc. (36.1% of estimated blood volume). Cannula wash and surgery 34 cc. (10.6%); samples —12 cc. (3.6%); total blood loss 162 cc. (50.5%).

This experiment shows the remarkable ability of an animal, which for 4.33 hours had had a low blood pressure with progressive hemodilution and oxygen and carbon dioxide reduction as a result of stimulation of the aortic-depressor nerves, to tolerate superimposed intermittent bleeding during an additional 2.16-hour period of continuous stimulation.

In the experiments represented in Table VIII, the animals were sacrificed by continuous bleeding after similar periods of low blood pressure from aortic-depressor nerve stimulation. In the first three experiments, the bleed-

ing was carried out with the stimulus still in operation. The behaviour under stimulation before bleeding was, in general, similar to that in the previous experiments, but when the animals were sacrificed by continuous bleeding, the volume obtained was appreciably less than that from controls and from those bled intermittently over a much longer period.

Figure 15, Rabbit 90, shows the blood pressure averaging about 55 Mm.Hg during a 4.3-hour period of stimulation throughout which there was a progressive hemodilution (Table IX) and weakening of the pressor response

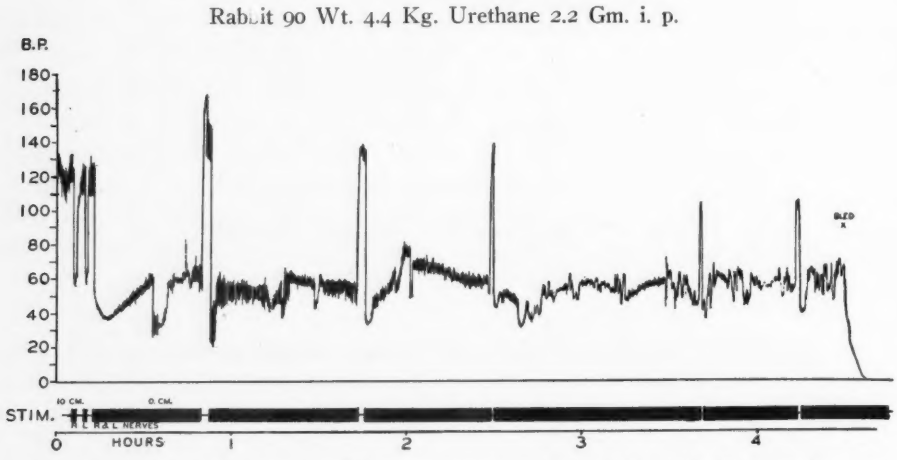


FIG. 15.—Vasodepression from aortic-depressor nerve stimulation with gradually decreasing vasomotor tone and terminal bleeding to death. Bleeding volume moderately reduced. Terminal bleeding 91 cc. (31%); cannula washings and surgery 12 cc. (4%); samples 12 cc. (4%); total blood loss 117 cc., or 39% of the estimated blood volume.

on release of the stimulus. The blood carbon dioxide was reduced and the oxygen was increased, this being the only experiment in which O_2 increase occurred. It might have been related in part to the rapid respirations which averaged 90 per minute after the first hour. The animal was bled 93 cc. to death, and lost 12 cc. in samples and 12 cc. in cannula wash—a total of 117 cc., or 39 per cent of the estimated blood volume. The reduction in bleeding volume would indicate that the previous period of vasodepression had somewhat impaired the ability of the animal to tolerate blood loss.

Figure 16, Rabbit 110, shows the blood pressure averaging 40 to 45 Mm. Hg for four hours (aside from two release periods) with a moderate hemodilution and only a slight reduction in pressor response during a seven-minute release of stimulus 30 minutes before the end. With stimulation continued, it required 20 minutes for bleeding 110 cc. to death. This amount, plus 13 cc. lost otherwise, gave a bleeding volume of 35 per cent, based on the calculated blood volume determined 24 hours before the experiment. The blood volume calculated after 2.75 hours showed a reduction of 21.4 per cent total volume, 12.5 per cent plasma volume and 33.33 per cent red cell mass. The hemodilution and reduction of circulating blood volume were responsible for the reduced bleeding volume.

In the last two experiments of Table VIII the stimulus was removed and a rest period allowed before bleeding to death.

Rabbit 102, weight 5.1 Kg., with an initial blood pressure of 100 Mm.Hg, had a prompt fall to 24 Mm. on stimulation of the left aortic-depressor nerve and the pressure ranged between 24 and 50 Mm. for three hours, averaging about 40 Mm. During the first half-hour there was occasional struggling, after which the animal became unresponsive. Blood dilution resulted as follows: red blood cells from 5.74 to 4.76, hematocrit 35 to 27.5, plasma proteins 6.25 to 4.94 Gm. per cent; blood oxygen 6.43 to 6.12, and carbon dioxide 21.94

TABLE VIII

PERCENTAGE OF BLOOD LOSS FROM CONTINUOUS BLEEDING NECESSARY TO CAUSE DEATH AFTER PERIODS OF LOW BLOOD PRESSURE FROM AORTIC-DEPRESSOR NERVE STIMULATION

Exp. No.	Wt. Kg.	Initial Pressure Mm. Hg.	Strength of Stimulus	Total Time Stimulated Hrs.	Pressure During Stimulation Mm. Hg.	% of Blood Volume Lost: From Bleeding	Surgery, Clot Wash and Samples	Total
With Stimulation On								
8 1	4.5	100	10–9 cm.	1.0	28–40	35.0	4.0	39
119	6.0	100	8 cm.	4.0	30–50	31.4	3.6	35
90	4.4	120	0 cm.	4.3	40–60	31.0	8.0	39
						32.5 Avg.	5.2 Avg.	37.7 Avg.
With Stimulation Off								
102	5.1	100	10–9 cm.	4.0	24–40 for 3 hrs. (3 hrs. rest followed) 26–30 for 5 hrs. (2.5 hrs. rest followed)	36	10	46
117	4.0	115	10–7 cm.	2.2	30–60 for 1.7 hrs. (0.5 hr. rest followed)	42	4	46
						39% Avg.	7% Avg.	46 Avg.

to 20.05. A blood volume determined during the last hour was almost the same as the control. (See Table V). The pressor responses on brief release of stimulus were only slightly reduced. Release of the stimulus at the end of three hours was followed by a rapid rise of the pressure to 110 Mm.Hg, where it continued and there was soon a resumption of struggling. Beginning three hours later the blood pressure was held at an average level of 30 Mm.Hg for 35 minutes by stimulation, during which time the animal again became quiet. After removal of the stimulus, the blood pressure promptly rose again and continued at an average level of 115 Mm. The animal again struggled and at the end of 1.5 hours was awake and cried when his wounds were disturbed. Vasodepression increased the degree of anesthesia and analgesia. An hour later, the animal was bled 120 cc. to death. The total blood loss during the experiment was 156 cc., or 46 per cent of the estimated blood volume, indicating little damage done to the circulation by the stimulation.

Rabbit 117, weight 4.0 Kg., on stimulation had a drop of blood pressure from 115 Mm. to 32 Mm.Hg. It gradually ascended during 2.2 hours to 60 Mm.Hg when the stimulus was removed. There was no significant blood change. On release of stimulus, the pressure quickly rose to 120 Mm.Hg where

Rabbit 119 Wt. 5.95 Kg. Urethane 3 Gm. i. p.

	RBC M	Hb. gms.	Hcr. %	CO2 Mm/L	O2 Mm/L	Plasma Proteins gms.%
1.	5.86	13.04	39.0	16.71	7.75	5.97
2.	5.77	12.42	36.0	13.76	7.17	5.15
3.	5.38	11.82	34.5	13.84	7.06	5.18

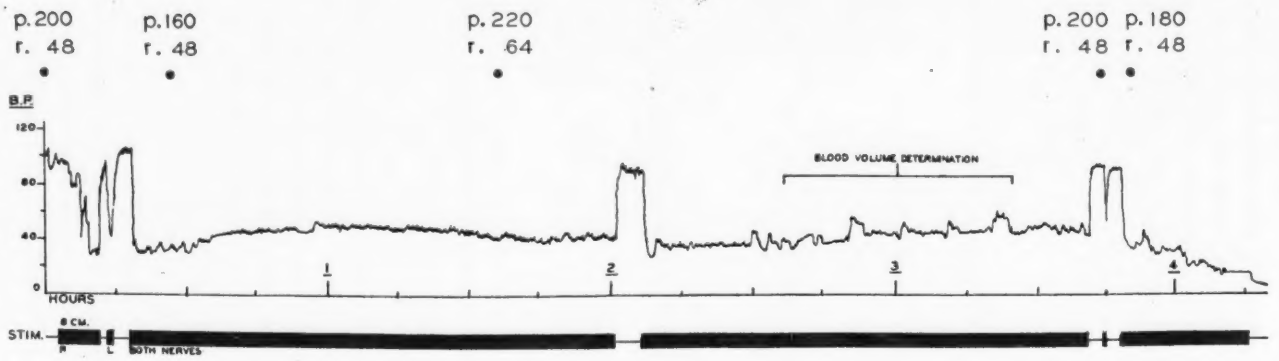


FIG. 16.—Vasodepression by aortic-depressor nerve stimulation for four hours. Vasomotor center little impaired. Bleeding volume moderately reduced (35 per cent) by hemodilution and reduced circulating blood volume.

it remained for one-half hour. The animal was then sacrificed by bleeding 115 cc. Eleven cubic centimeters of blood were lost during the experiment, giving a total of 126 cc., or 46 per cent of the estimated blood volume.

These experiments demonstrate that, in the rabbit, hemorrhage superimposed on a low blood pressure maintained for periods varying from one to four hours by vasodepressor nerve stimulation is relatively well tolerated. If the bleeding is continuous, the animal is killed by loss of a smaller amount of blood than if the bleeding is intermittent. In the latter case, and in case the stimulus is released and a rest period elapses before bleeding, the bleeding volume may be but little or no less than that of anesthetized animals bled without stimulation.

TABLE IX

RABBIT NO. 90 (FIG. 15)

Time Hrs.	R.B.C. M.	Hb. Gm.	Hcr. %	CO_2 Mm/L	O_2 Mm/L
Control	8.10	16.2	39.8	20.02	5.86
1.0	6.26	13.4	35.3	10.27	6.14
3.0	5.98	13.3	34.0	14.15	6.90
4.0	5.94	13.3	33.0	13.10	7.01
	Bled 93 cc. (31%) to death				

HEMORRHAGE TO SHOCK LEVELS FOLLOWED BY AORTIC-DEPRESSOR NERVE STIMULATION

In case of injury in man, there may be blood loss that is sufficient to lower the blood pressure to shock levels and then vasodepressor impulses, created by the psychological reaction to the distressing surroundings, may bring on syncope. A gunshot wound of the abdomen may injure blood vessels, resulting in shock from hemorrhage, and the surgeon during operation may produce an additional decline in pressure by intra-abdominal manipulation which sets up afferent depressor impulses. The effects in such clinical cases may be approximated experimentally by producing shock from hemorrhage and then superimposing a further fall of blood pressure by aortic-depressor nerve stimulation.

In six rabbits the nerves were prepared for stimulation and the animals then bled intermittently in varying amounts from 15 to 35 per cent of the estimated blood volume and to various shock levels of blood pressure ranging from 40 to 70 Mm.Hg. Nerve stimulation 15 to 45 minutes after the last bleeding produced an additional fall of blood pressure averaging 24 Mm.Hg (Table X). While the effects of the vasodepression from stimulation were not uniform, it usually appeared to shorten somewhat the period of survival as compared with controls (Table XI).

Figure 17, Rabbit 101, shows the effect of five bleedings at 15-minute intervals of 30 cc., 15 cc., eight cc. and seven cc., respectively, making a total of 91 cc., or 30 per cent of the estimated blood volume. Fifteen minutes after the last bleeding the blood pressure was slightly on the rise at 54 Mm.Hg. Stimulation beginning then lowered the pressure to 26 Mm., from which

level it gradually rose and then declined to death in one hour. Release of the stimulus at 24 minutes resulted in elevation of pressure to 70 Mm.Hg, which is an indication that the stimulation had so far done little harm, but a second release at 36 minutes showed a much smaller pressor response, which spoke for damage to the vasomotor center. The blood diluted markedly during the bleeding period but only slightly during stimulation (Table XII). Judging by the rapid change in vasomotor tone, the stimulation appeared to hasten death to some extent.

TABLE X

RABBITS BLED INTERMITTENTLY TO SHOCK LEVEL, WHICH WAS FOLLOWED BY FURTHER VASODEPRESSION FROM STIMULATION OF THE AORTIC-DEPRESSOR NERVES.

Exp. No.	Wt. Kg.	Initial Pressure Mm. Hg.	Time Required to Bleed	Total Amount Bled	Pressure Levelled: Within Min.	Pressure Levelled: At Mm. Hg.	Range of Pressure Levels During Stimulation	Survival Time After Stimulus Applied	Total Blood Loss Incl. Samples and Clot Wash
111.....	4.4	104	0.25 hr.	15.0%	30	70	46 to 68	2.0 hrs.	20.0%
107.....	4.7	110	0.25 hr.	17.5%	45	50	28 to 34	1.0 hr.	20.0%
101.....	4.5	120	1.0 hr.	30.0%	15	54	28 to 44	1.0 hr.	34.6%
92.....	5.1	100	0.25 hr.	20.0%	45	40	20 to 22	1.1 hrs.	25.5%
100.....	4.9	120	1.0 hr.	35.0%	20	50	26 to 30	0.4 hrs.	40.0%
Averages.....				23.8%				1.1 hrs.	28.0%
118.....	6.0	100	0.25 hr.	15.0%	30	60	16 to 34	7.5 hrs.	26.0%

TABLE XI

CONTROL INTERMITTENT BLEEDINGS TO SHOCK LEVEL

Exp. No.	Wt. Kg.	Initial Pressure Mm. Hg.	Bleeding to Shock Level: Time	Bleeding to Shock Level: %	Survival After Bleeding Hrs.	Total Blood Loss Inc. Samples and Clot Wash
120.....	4.0	96	0.5 hr.	20.0	1.8	20.0%
104.....	4.8	96	1.25 hrs.	25.0	1.5	34.0%
142.....	3.8	100	2.16 hrs.	30.0	1.5	30.0%
95.....	4.4	120	2.0 hrs.	33.0	0.5	40.0%
103.....	5.7	110	1.75 hrs.	37.5	3.1	44.0%
105.....	5.0	126	1.75 hrs.	40.0	0.8	44.0%
Group averages.....				30.9%	1.5	35.3%

TABLE XII

RABBIT NO. 101 (FIG. 17)

Time Hrs.	R.B.C. M.	Hb. Gm.	Hcr. %	CO_2 Mm/L	O_2 Mm/L
Control.....	4.92	11.3	34.6	17.90	6.76
0.33.....		Bled 91 cc. (30% of blood volume)			
1.33.....	3.72	8.8	25.0	7.95	5.14
1.66.....		Stimulus applied			
2.16.....	3.52	8.5	23.6	.....	....
2:5.....	3.37	7.9	23.0	4.64	4.60

However, Figure 18, Rabbit 118, illustrates the necessity of being cautious about concluding that vasodepression from nerve stimulation superimposed on low blood pressure from hemorrhage necessarily shortens the period of survival under stimulation. After bleeding 34 cc. and 15 minutes later, 17 cc., a total of 15 per cent of the estimated blood volume, the blood pressure leveled at 60 Mm.Hg one-half hour later. Stimulation was then begun and the blood pressure fell to 16 Mm.Hg. It slowly rose during the next 5.5

hours to 34 Mm. and then more rapidly declined until death at the end of two hours. Necropsy revealed gross evidence of congestion of spleen, liver and kidneys. Microscopically, the sinuses of the spleen were markedly congested (Figure 19). The kidney showed moderate congestion and necrosis of tubules (Figure 20). There was mild hepatic congestion and scattered necrosis of liver cells singly and in groups. The lungs contained little blood but there was protein precipitate in some of the alveoli. The adrenals, heart and skeletal muscle showed no changes.

Rabbit 101 Wt. 4.53 Kg. Urethane 2.25 Gm.

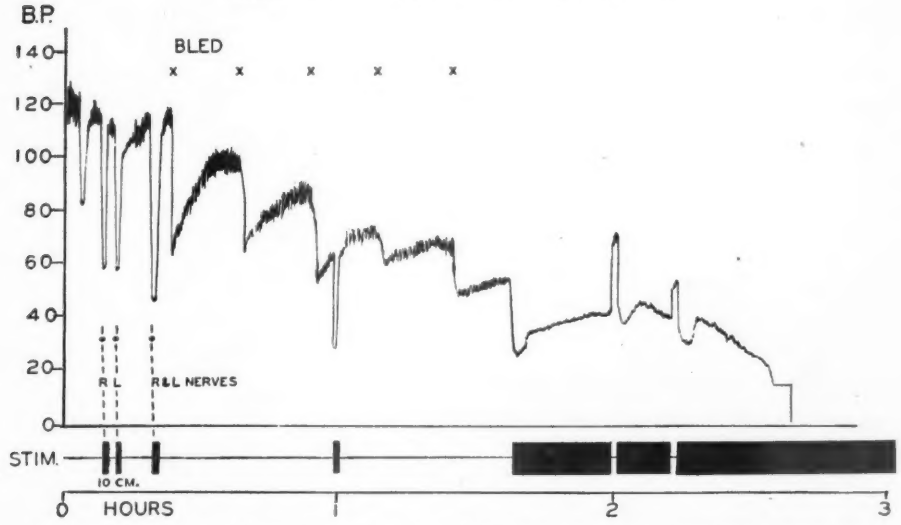


FIG. 17.—Intermittent bleeding to shock level followed by further vasodepression from aortic-depressor nerve stimulation which apparently shortened the time of impairment of vasomotor tone and shortened the survival period.

This 7.5-hour period of survival during nerve stimulation was longer than that of any of the entire series in which stimulation was not preceded by bleeding and in which the pressure was held at a similarly low level. In addition, 36 cc. of blood was lost from surgery, cannula washings and samples. The low blood pressure was due partly to the hemorrhage and partly to the stimulation but the vasomotor response on release held up remarkably well, considering the low level of pressure during the first half of the period of stimulation. Blood examination showed sharp hemodilution following the hemorrhages and moderate dilution during the period of stimulation (Table XIII).

An effect of marked lowering of blood pressure by aortic-depressor nerve stimulation observed incidentally was a tendency to deepening of the degree of anesthesia and analgesia as the period of vasodepression was prolonged. When the blood pressure was maintained at a low level continuously, the anesthesia and analgesia were observed to deepen gradually. When the stimulus was then removed, there was a gradual lessening in degree of both.

This is illustrated in Rabbit 102, and well shown in Figure 21, Rabbit 140.

Stimulation of the saphenous nerve in the latter animal produced a transitory fall and rise of blood pressure with a struggle and faint cry. The aortic-depressor nerve was then stimulated and the pressure fell sharply, to range between 26 and 42 Mm.Hg during a one-hour and five-minute period. Stimulation of saphenous nerve five minutes after the onset of vasodepression produced a struggle and faint cry but 40 and 52 minutes later it produced no response. Eight minutes after release of the depressor stimulus there was still no response to saphenous nerve stimulation, but 12 minutes later there was a mild struggle on stimulation. Cutting of the sciatic nerve then

TABLE XIII

RABBIT NO. 118 (FIG. 18)

Time Hrs.	R.B.C. M.	Hb. Gm.	Hcr. %	CO_2 Mm/L	O_2 Mm/L	Plasma Proteins
.0	6.32	12.0	36.8	15.34	7.08	6.37
1.5	6.00	11.7	36.0	12.40	7.01	5.82
1.5	Bled 34 cc. (10% of estimated blood volume)					
1.75	5.62	10.8	32.5	12.14	6.54	5.51
1.75	Bled 17 cc. (5% of estimated blood volume)					
2.16	Stimulus applied					
4.16	4.96	9.53	28.7	7.87	5.68	4.88
7.16	4.90	9.45	28.7	.....	....	....
9.5	4.78	9.20	27.9	.....	....	....

produced a struggle, as did stimulation of it five minutes later. A second period of 1.25 hours of vasodepression was then produced. Fifteen minutes after the onset, sciatic nerve stimulation produced a struggle, but 50 minutes later the response was very feeble and in one hour it had disappeared. Five minutes after release of the aortic nerve stimulus and recovery of the blood pressure, there was a very faint response on sciatic stimulation, and in 40 minutes the response was of moderate degree. It appears that the cerebral cortical centers may be affected in advance of the vasomotor center.

SOMATIC NERVE IMPULSES

In case of accidental wounds afferent nerve impulses from the injured field that result in reflex lowering of blood pressure may pass over two sets of fibers. Afferent depressor impulses may pass to the vasomotor center in the medulla where they affect directly the vasodepressor mechanism. Pain impulses go to the cerebral cortex where in the conscious subject they frequently produce an adverse psychic effect that in turn results in a severe decline of blood and fainting from the passage of vasodepressor and cardiac inhibitor impulses from brain to medulla.

Clinical interest in these reactions centers in whether or not they may be of sufficient magnitude and duration to become a factor in the production of shock. Anesthesia precludes reflex vasodepression produced by painful impulses. Consequently, any fall in blood pressure produced by depressor nerve impulses from the injured field during operations on man under general anesthesia or in experiments on anesthetized animals would result from such impulses passing directly to the vasomotor center in the medulla. Both

animal experimentation and recent clinical experience in which the shock factor of blood and plasma loss is carefully guarded against by blood and plasma transfusions indicate that this mechanism is of little or no importance in the production of shock. A possible exception is abdominal manipulation in which there may be a fall of blood pressure by a mechanism that is imperfectly understood.

Rabbit 118 Wt. 4.95 Kg. Urethane 2.5 Gm. i. p.

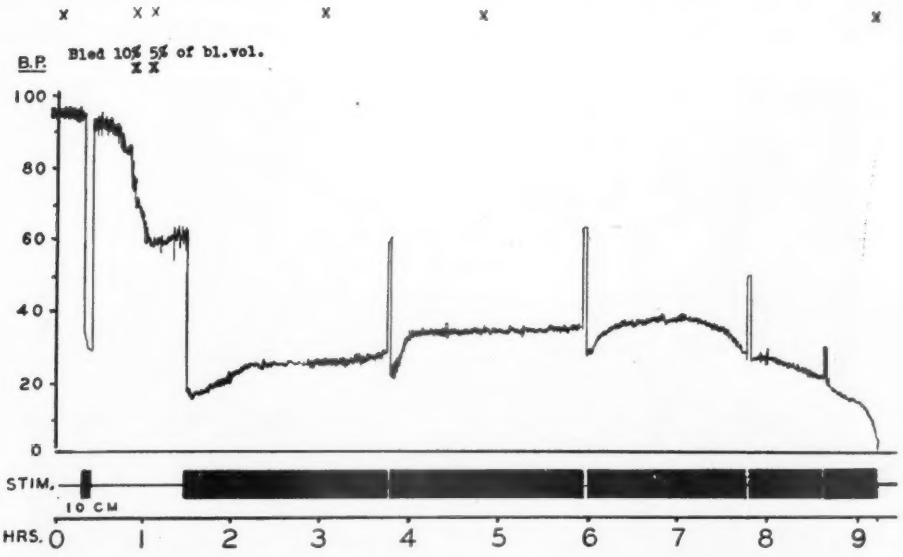


FIG. 18.—Rabbit 118: Small intermittent bleeding to shock level followed by further severe and extremely prolonged vasodepression from bilateral aortic-depressor nerve stimulation.

In animal experiments[11, 12, 13, 14] the direct exposure and stimulation of the central end of various somatic nerves of the extremities by electric currents of different strengths and frequencies produce a variety of pressor and depressor reactions. Most of them are of small magnitude and of brief duration, some examples of which are seen in Figure 21, Rabbit 140. Prolonged stimulation with either tetanizing or slow make and break shocks has not been demonstrated to produce a prolonged and sustained lowering of blood pressure and nothing remotely resembling a state of shock has resulted. On the contrary, with the stronger tetanizing currents after the initial sharp fall and rise or rise only, the blood pressure may either return to the former level or remain slightly elevated throughout a period of one or more hour's stimulation.

The effect on blood pressure of stimulation of the saphenous and sciatic nerves was determined in 12 rabbits, since this animal had been little used in reported experiments. The results were essentially the same as those reported for other animals. The result of only one experiment is included here.

Figure 22, Rabbit 152, illustrates the effect of three stimulation periods of approximately 1.25 hours duration by means of a shield electrode applied to the right sciatic nerve, with the secondary coil of the inductorium placed at eight cm. from the primary. Onset of stimulation produced a relatively slight depression, then elevation and immediate return of pressure to pre-stimulation level of 100 Mm.Hg. After 1.16 hours, the pressure had declined to 78 Mm. and the stimulus was removed. No change in elevation occurred. Within 25 minutes, the pressure had risen to 82 Mm. The electrode was then adjusted and stimulus again applied for one minute and the same type of deflection occurred as was obtained at the start except that the degree was slightly

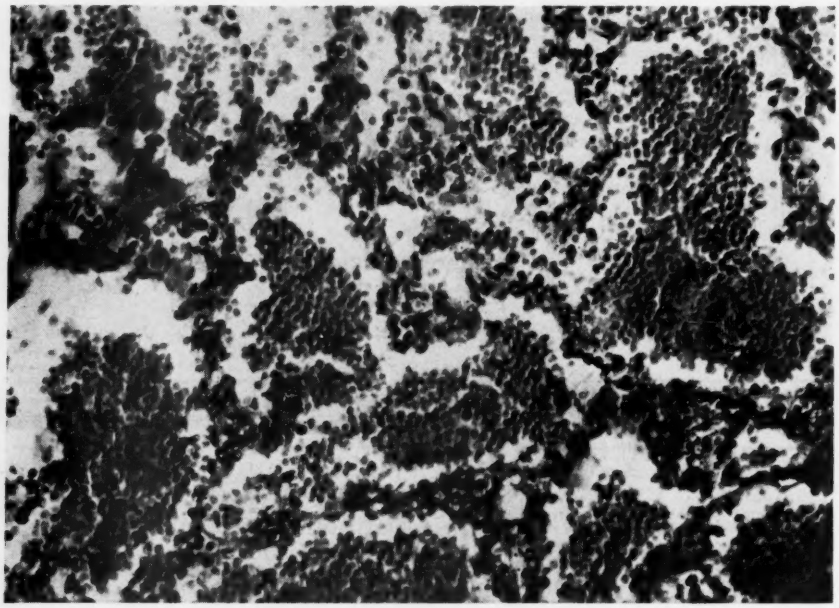


FIG. 19.—Rabbit 118: Congestion of spleen. (× 450)

greater. Beginning five minutes later, another 1.16-hour period of stimulation was given but very little pressure change resulted, the level dropping only from 82 to 78. An hour and a half rest followed, the pressure leveling at 86, and the stimulus was again applied at the same strength, producing a faint cry but no deflection. After 15 minutes the pressure had again dropped to 78 and the stimulus strength was increased to four cm. The pressure rose sharply to 100, declined to 80 in five minutes and reached 70 Mm.Hg 20 minutes later, from which point it slowly rose to 74 within the next hour. The stimulus was then removed, and as no appreciable change occurred within the next 50 minutes, the animal was sacrificed.

Mechanical stimulation of the saphenous and sciatic nerves was produced by repeated pinching and crushing by means of a hemostat. The usual reaction to such strong stimulation was a quick rise in blood pressure of ten to 25 Mm.Hg, with a decline to the vicinity of the previous level in two or

three minutes, and continued pinching would fail to keep the pressure significantly elevated.

Stimulation was also carried out by rubbing and pinching the surfaces of large wounds made in the neck and thighs to resemble a severe accident. Small nerve fibers and effector organs were the structures stimulated and the response was variable but less pronounced than when large trunks were directly involved. Frequently the manipulations would produce a fall and rise in blood pressure of 15 to 20 Mm.Hg, lasting two or three minutes, following which the pressure remained at the previous level although the manipulations were continued. Sometimes there would be a brief decline followed by a rise,

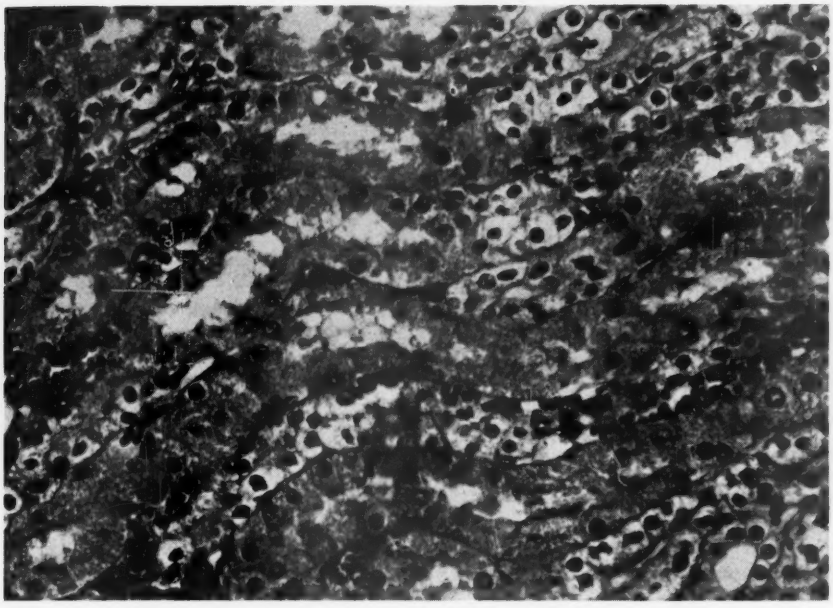


FIG. 20.—Rabbit 118: Mag. 500 dia. Congestion of kidney and necrosis of tubules. (× 500)

or occasionally the order would be reversed, but in no case was a prolonged lowering of blood pressure produced in this way.

In man the cutting, pinching, crushing and stretching of a large nerve as the sciatic has been continued for a few minutes during amputations. The procedure produces a slight rise in blood pressure and shock is not a sequela. Gentle handling of tissues during operations has long been advocated for the avoidance of shock that may arise from stimulation of the nerves in the field. Gentle handling is a very valuable teaching as it reduces trauma to the tissues, exudation into, and infection of, the wounds and favors wound healing. However, there is no well controlled evidence that it lessens the incidence of shock by decreasing the afferent depressor nerve impulses set up in the wound, except possibly in connection with upper abdominal operations.

It has been reported by O'Shaughnessy and Slome,[15] and by Lorber, Kabat and Welte,[16] that when a lower extremity of a dog has been severed except for the nerves and femur and the circulation maintained by either crossed circulation or perfusion with blood rendered noncoagulable, trauma then applied to the leg will cause the animal to have a decline in blood pressure and go into shock more readily than if the nerves had also been severed. Blalock and Cressman[17] did not confirm these results except to report that spinal anesthesia reduced the tendency to shock when it was followed by general anesthesia produced by nembutal in cats and chloralose in dogs.

It is difficult to conceive a reason why nerve impulses capable of lowering blood pressure and producing shock would arise in the traumatized field of such a leg while direct electrical or mechanical stimulation of the proximal

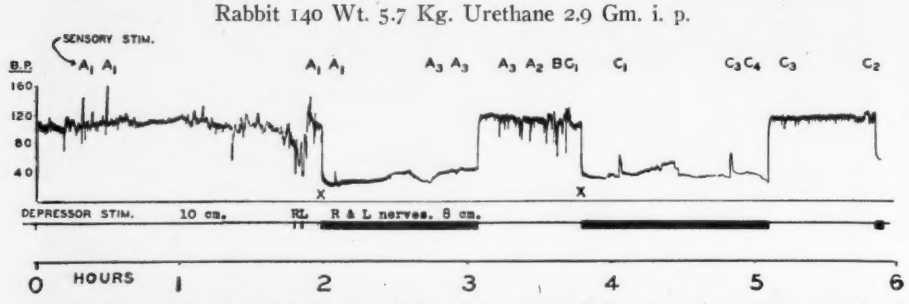


FIG. 21.—Somatic nerve stimulation with tetanizing current before, during, and after periods of vasodepression produced by stimulation of the aortic-depressor nerve. A—Saphenous nerve stimulation; A_1—Struggles marked; A_2—Mild; A_3—None; B—Sciatic nerve cut; C—Sciatic nerve stimulated; C_1—Struggles marked; C_2—Moderate; C_3—Slight; C_4—None.

end of the divided sciatic nerve fails to create such impulses. Parsons and Phemister[18] found that denervation of the limb made no difference in the results when shock was produced by trauma to the lower extremity of the dog, the effect being due to local loss of circulating fluid.

Discussion.—The outstanding feature of the aortic-depressor nerve stimulation experiments was the remarkable ability of the animals to tolerate long periods of low blood pressure produced by afferent depressor impulses without serious impairment of the circulation. When the stimulation producing vasodepression was continued the blood usually became diluted, as indicated by a gradual reduction in red cells, hematocrit, hemoglobin, plasma proteins, and oxygen and carbon dioxide content. In animals which died after a more prolonged period of vasodepression the necropsy findings revealed tissue damage from the hemodilution and anoxia. Some of the organs were congested and acute degenerative changes were found in the liver and kidneys.

The vasomotor center proved to be very resistant as shown by the prompt elevation and decline of pressure with each brief release of the stimulus. Failure of response developed gradually in the late stages of those experiments in which stimulation was continued until death. Both the hemodilution with

its anoxia and the stimulation appeared to damage the center and in some cases the latter was the more important factor, as shown by Figure 10, Rabbit 133. After three hours of marked vasodepression there was very feeble pressor response on release of the stimulus whereas a blood sample taken at the same time revealed extremely little hemodilution. Early death in Rabbit 147 (Fig. 4) appeared to be due mainly to the stimulus which was produced by a relatively strong current.

FIG. 22.—Sciatic nerve stimulation with continuous tetanizing current at three intervals approximately 1.25 hours each.

In some experiments prolonged release of the stimulus after hours of vasodepression to shock levels was followed by prompt return of the pressure to the previous level and the animal lived on much as if no stimulus had been applied. Also the blood which becomes diluted during the vasodepression may subsequently concentrate as shown in Figure 9, Rabbit 79.

The circulating blood volumes determined on five rabbits are probably only roughly accurate because of the variable conditions of the experiments and the inadequacy of the dye method. However, it appears from the data presented in Table V that any change in volume is in the direction of a slight decrease since the plasma volume was reduced in every experiment except one. The much reduced red cell mass appeared to be the result of trapping of cells in various structures as the spleen. In order to reconcile the coexistence of hemodilution and reduced circulating blood volume it is necessary to assume a loss of both plasma and water from the circulating blood which may be the result of capillary damage. Further studies on the water and electrolyte equilibria between blood and tissues and of the morphologic changes, including the central nervous system, are indicated.

Blood transfusion improved the circulation that had been impaired by prolonged vasodepression through nerve stimulation by increasing the circulating blood volume and the blood concentration. Plasma transfusion had a similar influence due to the increase in circulating volume and elevation of plasma proteins even though there was a further diminution of red cells, hemoglobin and hematocrit (Fig. 13).

Bleeding after prolonged periods of low blood pressure from aortic-depressor nerve stimulation was somewhat damaging but relatively well tolerated, as indicated by the bleeding volumes that were obtained when the

animals were bled to death (Tables VI and VIII). Bleeding to shock levels before further lowering the blood pressure by stimulation of the aortic-depressor nerves tended to shorten the survival period to some extent (Table X).

In contrast with the marked and prolonged lowering of blood pressure and failure of the circulation which could be produced by aortic-depressor nerve stimulation, was the complete failure to produce such effects by direct exposure and stimulation of somatic nerves by pinching, crushing and use of electric currents of various strengths and frequencies.

Syncope[19] or fainting is the only definitely established condition in man in which afferent depressor impulses produce a rapid and marked fall of blood pressure closely approximating that produced in the rabbit by aortic-depressor nerve stimulation. But fainting is a relatively short lived condition. With loss of consciousness the subject passes to the recumbent position bringing heart and brain to the same level. The circulation to the brain is thereby improved, the adverse psychic reaction is dispelled, the blood pressure rises and consciousness is regained within a few minutes. The experiences of the clinic and of every day life show that fainting *per se* produces only temporary embarrassment of the circulation and does not lead to shock.

Manipulations during upper abdominal operations[20, 21] sometimes produce a fall in blood pressure and bradycardia that appear to be the result of afferent depressor nerve impulses but their pathways are as yet not well understood. Numerous observations by one of us (D. B. P.) indicate that such a fall in blood pressure in man is usually short-lived and passes off without damaging the circulation. However, the low blood pressure occurring either in syncope or from abdominal manipulations if combined with a low blood pressure from hemorrhage might help to produce shock as did hemorrhage combined with aortic-depressor nerve stimulation in rabbits.

The pathologic report of the tissues was kindly furnished by Dr. Eleanor Humphreys.

SUMMARY AND CONCLUSIONS

1. Stimulation of the aortic-depressor nerve of the rabbit may maintain the blood pressure at shock levels for hours without serious impairment of the circulation or of the body tissues. However, if continued for a longer period it may produce death from the effects of hemodilution, anoxia and damage to the vasomotor centers, a condition which may be designated as neurogenic shock. Plasma proteins are lost from the blood apparently as a result of capillary damage.

2. Judging by the relative harmlessness of these long periods of low blood pressure in rabbits, by the inability to produce more than a brief slight lowering of blood pressure by direct stimulation of somatic nerves which carry impulses from traumatized fields and by the comparatively short duration of the periods of reflex lowering of blood pressure during syncope

and abdominal manipulations, it is extremely improbable that "primary shock" is ever produced in man by the action of afferent depressor nerve impulses.

3. The use of the term "primary shock" to denote such a condition should be abandoned.

4. When the blood pressure of the rabbit was first lowered to shock levels by hemorrhage and the aortic-depressor nerve then stimulated, the additional lowering of blood pressure would tend to hasten death to some extent. Also when the blood pressure was first maintained at shock levels for periods of one to four hours by aortic-depressor nerve stimulation and the rabbits then bled, there was usually some reduction in ability to tolerate blood loss.

5. Judging from the results of combining hemorrhage and aortic-depressor nerve stimulation in lowering blood pressure and producing shock in rabbits, the occurrence in man of fainting or of a reflex fall of blood pressure from abdominal manipulation in the presence of low blood pressure produced by hemorrhage may constitute a contributing factor to shock. Clinical experience also supports this contention to some extent.

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STUDIES ON TRAUMATIC SHOCK: I—BLOOD VOLUME CHANGES IN TRAUMATIC SHOCK*

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DURING WORLD WAR I there was ample opportunity for a serious clinical study of traumatic shock. Many observations were made by competent groups of researchers in both the English and American medical corps. The experiences of these groups were reported by the joint English and American Research Councils, but the material was made more generally available by the publication of Cannon's[1] important monograph "Traumatic Shock" in 1923.

Since that time, although the remarkably thorough and painstaking investigations of Blalock directed attention to the importance of local blood loss as a causative factor in traumatic shock, no studies have been made on the blood volume of patients in shock as a result of trauma.

With the advent of the present global war, attention was again drawn to the urgent need for more data on clinical shock. By this time accurate clinical observations could be correlated with the blood volume of patients in shock because of the development of an adequate method by Gregersen, in 1935, for the estimation of plasma volume.

The present communication is a report of the estimation of plasma volume in a considerable number of patients in shock as a result of various types of trauma, and an attempt to correlate these blood volume studies with the manifestation of shock signs in these patients. We have tried to determine the relative importance of blood loss as an initiating and sustaining factor in traumatic shock.

We are fortunate in having at our disposal a considerable amount of clinical shock material very similar to the shock-patient group seen in modern warfare. One of our hospitals cares for a large urban Negro population, mostly of lower economic levels. The injuries sustained by these persons are caused, in general, by knife and gunshot wounds of the extremities, chest and abdomen. To this group of shock cases has been added a considerable number of traumatic injuries of the skeletal structures caused by automobile and industrial accidents.

THE ESTIMATION OF PLASMA VOLUME IN THE SHOCK STATE

There has been considerable hesitancy on the part of research workers

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CHART 1

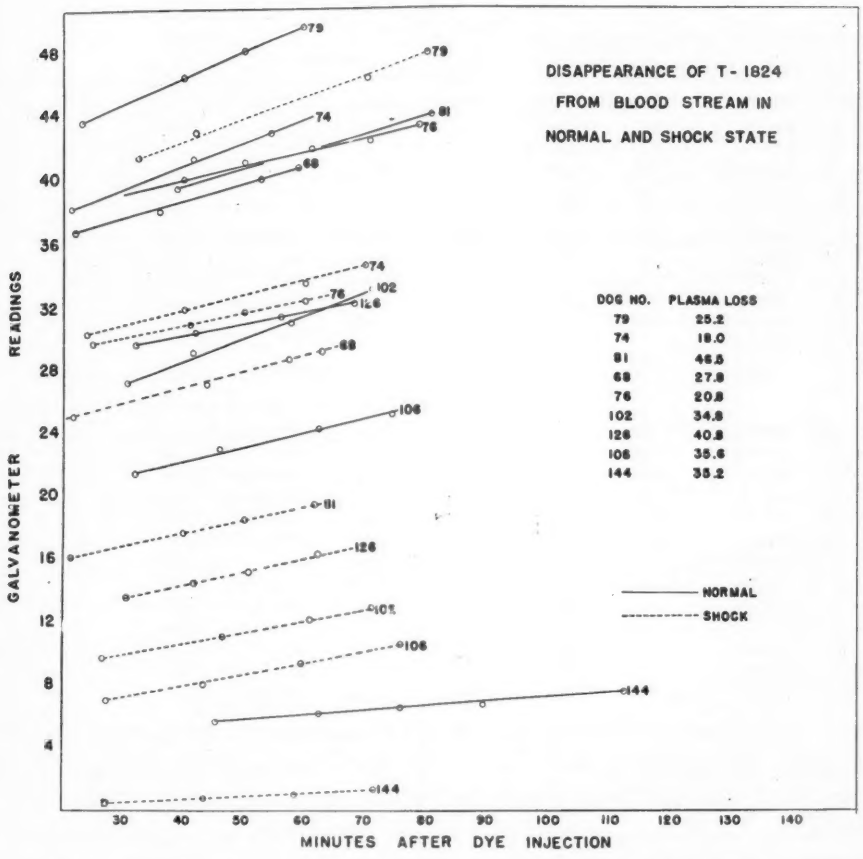

CHART 1.—Disappearance rate of dye T-1824 from the blood stream of dogs, during normal state and in shock from intestinal strangulation. The disappearance rates are practically identical, suggesting that there was no generalized increase in capillary permeability in the shock state.

to attempt the determination of plasma volume in the shock state, because of the current belief that there is in shock an increased capillary permeability. This generalized increase of capillary permeability, some maintain, will cause the injected dye to be lost from the vascular system into the tissue spaces rapidly, and in amounts great enough to seriously disturb the disappearance curve of the dye.

Insofar as we can find, the first determinations of plasma volume during the shock state were made by Keith,[2] and Robertson and Bock,[3] working for the Shock Committee during World War I. These investigators employed the vital red dye method of Keith, Rowntree and Geraghty,[4] and were able to demonstrate a rather serious depletion of plasma volume in wounded soldiers suffering from traumatic shock.

Following World War I, interest in the determination of plasma volume waned, probably due to the fact that considerable doubt was cast on the validity of the vital red method for the determination of plasma volume,

TABLE I

ACUTE BLOOD LOSS

Patient	Blood Pressure	Pulse Rate	Pulse Quality	Venous Filling	Extremities: Temp.	Extremities: Sweat.	Plasma Volume	Hemato-crit	Plasma Protein
Shock—None or Mild									
B. E.	110/80	120	Good	Good	Warm	Dry	39	42	6.8
B. N.	118/80	112	Poor	Poor	Cold	Dry	41	34	6.4
M. C.	100/60	92	Good	Good	Warm	Dry	38	31	7.7
J. R.	90/60	76	Poor	Good	Warm	Dry	45	43	6.8
A. C.	110/80	76	Good	Good	Warm	Dry	41	41	6.8
J. F.	80/60	68	Good	Poor	Warm	Moderate	38	39	5.7
R. A.	100/60	82	Fair	Good	Warm	Dry	42	39	6.6
J. H.	120/80	80	Good	Good	Warm	Dry	41	40	6.5
C. C.	92/66	80	Fair	?	Cold	Moderate	35	42	6.6
J. R.	68/48 to 130/90	64	Good	Good	Warm	Dry	42	32	5.4
A. S.	92/70	96	Good	Good	Warm	Dry	35	44	6.9
Moderate or Severe									
L. H.	Unobt.	160	Poor	Poor	Cool	Moderate	20	32	5.4
B. P.	90/60	150	Poor	Poor	Cool	Dry	28	27	6.6
V. B.	45/0	130	Poor	Very poor	Cold	Marked	24	34	6.9
D. G.	75/50	126	Fair	Good	Cold	Moderate	28	24	7.1
M. K.	65/50	120	Poor	Very poor	Cool	Marked	26	31	6.6
L. D.	68/58	130	Poor	Poor	Warm	None	26	28	6.9
O. S.	80/60	72	Fair	Poor	Warm	Dry	25	27	4.9
A. R.	60/40	80	Poor	?	Warm	Marked	33	41	6.3
W. R.	80/50	108	Poor	Poor	Cool	Dry	31	44	6.8
C. J.	65/20	90	Poor	Poor	Cold	Marked	26	35	6.0
T. D.	110/80	130	Fair	Poor	Cold	Dry	28	45	5.5
A. G.	80/40	92	Fair	?	Warm	Dry	31	35	6.7
C. G.	62/20	90	Fair	Fair	Warm	Marked	38	35	6.0

even in the normal state. It was not until Gregersen[5] developed and standardized the dye method which employs the dye T-1824, called by some "Evans' blue dye," that much recent work has been done on the determination of plasma volume. Gregerson, Gibson and Stead,[6] employing the spectrophotocolorimeter, were able to show conclusively that estimations of plasma volume could be made by this method if it were used in the manner outlined by them. Later, Gibson and Evelyn[7] adapted this method to use the Evelyn photoelectric colorimeter; this, in the minds of some, has simplified considerably the estimation of plasma volume.

There have been few published studies on the use of the Gregersen-Gibson method for the determination of plasma volume during the shock state. The observations of Freeman, and his coworkers,[8] who used this method in experimental shock produced by continuous adrenalin infusion, have cast some doubt on the validity of the T-1824 method for the determination of plasma volume during shock. These workers found the dye in the pericardial lymph and other tissue fluids; one could infer from their observations that there might be rather disturbing losses of the dye from the vascular system during shock, losses possibly so great as to disturb seriously the disappearance curve of the dye.

The majority of our observations with the Gregersen-Gibson method for the estimation of plasma volume during the shock state have been made in patients in clinical traumatic shock and in the experimental shock prepara-

tion, described earlier by one of us,[9] namely, the production of shock by the strangulation of a short loop of ileum.

In Chart 1 is shown the dye disappearance curves in ten dogs in the normal and in the shock state. The solid line represents the disappearance curve of the animal in the normal state while the broken line represents the dye disappearance curve for the same animal after it had lost enough plasma to put it into more or less severe shock. At the right of each disappearance curve is given the number of the animal. It will be noted that the dye disappearance curves in both the shock and normal state practically parallel each other for the same animal.

In Chart 2 are given a small number of dye disappearance curves for human patients in severe shock compared with several disappearance curves found in patients with normal blood volumes. It will be seen that the dye disappearance rate is practically the same whether the patient is in severe shock or not. In several instances in patients in severe traumatic shock we have found increased dye disappearance rates. However, when the plasma volume determination was carried out on the following day we would often get a high dye disappearance rate even though the patient then showed no evidence of clinical shock.

CHART 2

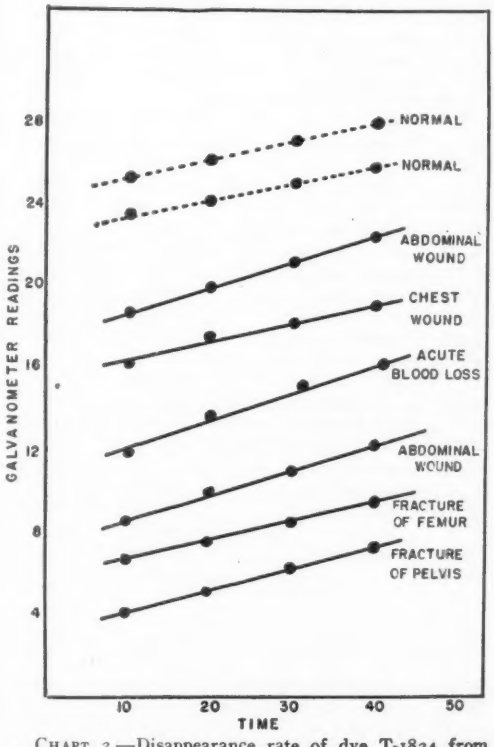

CHART 2.—Disappearance rate of dye T-1824 from the blood stream of human subjects during the state of traumatic shock.

Our experience with the use of the Gregersen-Gibson method for the estimation of plasma volume in well over 500 plasma volume determinations in the shock and normal states in patients has convinced us that the method gives valid data for the estimation of plasma volume during the shock state. The dye disappearance rates in clinical shock offer no evidence that would lead us to believe that there is generalized increased loss of the dye through the capillary wall in clinical traumatic shock.

Analysis of many dye disappearance rates in normal and shock patients has convinced us that for clinical purposes one can estimate plasma volume rapidly by using only one plasma sample, taken ten minutes after the injection of the dye. This, likewise, has been the experience of Gregersen, and his coworkers,[10] and Shaefer.[11] Throughout this research, however,

TABLE II

SKELETAL TRAUMA

Shock—None or Mild

Patient	Diagnosis	B.P.	Pulse Rate	Pulse Quality	Extremities: Venous Filling	Extremities: Temp.	Extremities: Sweat.	Plasma Volume	Hemato-crit	Plasma Protein
P. J.	Compd. fract. tibia, fibula	140/80	72	Good	Good	Warm	Dry	39	42	7.0
D. T.	Fract. femur	120/80	80	Good	Good	Warm	Dry	45	42	7.0
A. O.	Fract. pelvis	110/70	90	Good	Good	Warm	Dry	38	40	6.7
M. N.	Compd. fract. tibia, fibula	124/82	90	Good	Good	Warm	Dry	39	37	6.5
O. R.	Compd. fract. femur, tibia	110/68	60	Good	Good	Warm	Dry	42	47	7.0
H. C.	Fract. femur	128/80	80	Good	Good	Warm	Dry	46	46	7.7
E. T.	Gunshot wound, compd. fract. of shoulder	120/80	76	Good	Good	Warm	Dry	40	43	7.2
F. B.	Fract. tibia, fibula	90/50	80	Fair	Fair	Warm	Dry	40	34	7.0
I. D.	Fract. pelvis	120/70	90	Good	Good	Warm	Dry	45	39	7.2
T. D.	Fract. femur	130/80	84	Fair	Good	Warm	Dry	43	43	7.5
F. F.	Dislocated hip	130/90	90	Good	Good	Warm	Dry	31	47	6.9
M. M.	Fract. femur, knee laceration	110/65	104	Fair	Fair	Sl. cool	Dry	32		6.7
S. T.	Compd. fract. tibia, fibula	142/110 to 90/50	112	Fair	Good	Warm	Dry	29	34	7.2
J. C.	Fract. femur tibia, fibula	90/60 to 110/60	72	Good	Good	Warm	Dry	35	37	7.0
G. S.	Compd. fract. of femur	90/60	70	Good	Good	Warm	Dry	38	46	6.3
R. M.	Fract. of femur	96/64	100	Fair	Fair	Cool	Dry	25	33	6.1
S. H.	Compd. fract. of femur	80/60	100	Fair	Fair	Cold	Moderate	32	49	7.1
A. J.	Fract. femur	184/90	80	Good	Good	Warm	Dry	48		6.9
C. W.	Fract. femur	110/80	88	Good	Good	Warm	Dry	40	38	7.0
L. H.	Traumatic amp. of arm	130/90	82	Good	Good	Warm	Dry	41	44	6.2
E. M.	Fract. femur, basal skull fract.	120/80	78	Good	Fair	Warm	Moderate	43	40	6.5
L. A.	Gunshot wd., fract. femur	90/70	76	Fair	Good	Warm	Dry	42	40	7.0
J. C.	Fract. femur, radius & ulna	70/58	65	Good	Fair	Warm	Dry	45	33	5.3
W. F.	Compd. fract. tibia, fibula	120/80	..	Good	Good	Warm	Dry	42	44	6.7
E. W.	Fract. pelvis	110/70	..	Good	Fair	Warm	Dry	38	40	6.9
P. H.	Fract. pelvis	130/80	..	Good	Good	Warm	Dry	42	39	7.1
J. A.	Fract. femur	130/90 to 80/60	80	Good	Good	Warm	Dry	32	43	7.7
J. B.	Fract. femur	80/60 to 110/60	96	Good	Good	Warm	Dry	36	46	7.5

Moderate Shock

B. L.	Fract. femur	90/60 to 70/50	56	Poor	Good	Warm	Dry	28	36	6.3
L. F.	Fract. femur, scapula	90/60	80	Good	Good	Cold	Marked	25	48	6.8
E. S.	Compd. fract. tibia, fibula	136/68	118	Good	Good	Warm	Marked	31	39	5.9
R. H.	Fract. femur	70/45	100	Fair	Fair	Cool	Moderate	25	42	6.1
T. L.	Compd. fract. tibia, fibula	92/50	76	Good	Good	Cool	Dry	25	48	6.6
J. H.	Compd. fract. of femur	60/40	60	Poor	Fair	Cold	Dry	31	49	6.5
G. R.	Fract. tibia, fibula	80/40	80	Poor	Fair	Cold	Dry	31	39	6.9
N. F.	Fract. pelvis, & scapula	104/60	120	Poor	Poor	Cold	Marked	31	31	6.0
T. W.	Fracture of pelvis	70/50	136	Poor	?	Cold	Marked	36	38	6.1
L.M.S.	Traumatic amputation ft., compd. fract. tibia & fibula	75/40	68	Fair	?	Cool	Marked	32	43	6.6

Severe Shock

H. L.	Traumatic amp. of leg	130/50 to 70/50	100	Fair	Good	Cold	Marked	29	38	5.9
P. R.	Fract. pelvis	80/60	110	Fair	?	Cold	Marked	25	47	7.5
D. H.	Fract. femur & fibula	70/50	110	Poor	Poor	Cool	Marked	30	39	5.6
J. W.	Compd. fract. of tibia, fibula, fract. pelvis	125/60 to 75/50	110	Good	Good	Warm	Dry	25	31	7.3
H. G.	Compd. fract. of femur	58/40	140	Poor	Very poor	Cold	Marked	26	38	6.0

TABLE II—(*Continued*)

Patient	Diagnosis	B.P.	Pulse Rate	Pulse Quality	Extremities: Venous Filling	Extremities: Temp.	Extremities: Sweat.	Plasma Volume	Hemato-crit	Plasma Protein
J. W.	Fract. both ankles, compd. fract. of humerus	80/50	108	Very poor	Poor	Cool	Moderate	32	42	6.9
C. H.	Compd. fract. both tibia, fibula	165/95 to 120/80	100 to 136	Fair	Fair	Cold	Moderate	26	44	5.4
F. L.	Compd. fract. tibia, fibula; fract. of humerus	60/?	130	Poor	?	Cold	Dry	25	46	6.9
E. K.	Compd. fract. tibia, fibula	82/70	116	Poor	?	Warm	Dry	18	44	7.1
H. M.	Crushed pelvis	60/40	160	Poor	Poor	Warm	Dry	26	33	6.6
S. C.	Fract. femur & pelvis	88/60	100	Fair	Poor	Cold	Dry	25	38	?
R. T.	Fract. pelvis & unobt. femur		120	Poor	Fair	Cold	Dry	24	?	?
E. G.	Multiple compd. fract. of legs, fract. pelvis	90/60	88	Poor	Poor	Cool	Dry	28	?	?
L. G.	Fract. femur	80/40	90	Fair	Poor	Cool	Moderate	26	32	5.4
H. T.	Comp. fract. femur	80/45	108	Poor	Fair	Cool	Dry	35	42	6.7
W. C.	Fract. tibia, fibula	70/30	110	Poor	Poor	Cold	Moderate	28	42	?
A. T.	Fract. femur & lumbar vertebra	56/0	90 to 150		Poor?	Cool	Dry	22	?	?

we have tried to get at least four to six samples after the injection of the dye, so that we could estimate the dye disappearance rate.

Of importance is the fact that in this study all blood samples were taken without the use of the tourniquet. In patients in severe shock it is necessary to draw the blood samples from either an artery or the femoral vein. It has been our custom recently to use the femoral vein for blood sampling almost routinely in patients in severe shock so that the blood is drawn without any stasis.

Hematocrit estimations were made using the Sanford-Magath six-cubic centimeter graduated centrifuge tube; total protein was determined by the Kagan[12] method, which employs the falling-drop principle.

THE RELATION OF PLASMA VOLUME TO CLINICAL SHOCK

A well-organized city ambulance service enables us to observe our shock patients fairly soon after the injury has been received, as a result of which we have been dealing largely with patients in relatively early shock. The patients were brought directly to the Emergency Rooms, where they were placed immediately on a stretcher in the head-down position. No treatment was administered until after the arrival of a member of the "shock team" who were on 24-hour call. As soon as a hasty diagnosis and estimate of the likely severity of shock was established, a plasma volume determination was begun.*

During the time required to secure serial blood samples, clinical observations on the early signs of shock were made and recorded. These observations will be discussed in a subsequent section of this paper.

For convenience of analysis and presentation, we have classified our shock cases into four groups: (1) Acute blood loss; (2) skeletal trauma;

* We are grateful to Dr. Marvin Thompson of the Warner Institute for Therapeutic Research for liberal supplies of the dye T-1824.

(3) abdominal injuries; and (4) chest injuries. In the early part of this clinical study, we were called to see only patients in actual shock, but soon it became obvious that we should attempt to see and study all patients who had suffered severe traumatic injury, whether or not signs of shock were present. Thus, we are able to compare two groups of patients: (a) Those who had no signs of shock or only signs of mild shock; and (b) patients in moderate or severe shock. In general, the types of injury were the same in both groups. (See Tables I-IV)

The *acute blood loss* group is made up of those patients who suffered more or less severe loss of blood from lacerations of peripheral arteries and veins (usually as a result of knife or razor wounds). These wounds were not complicated by muscle trauma. The *skeletal trauma* group consists of all

CHART 3
Acute Blood Loss

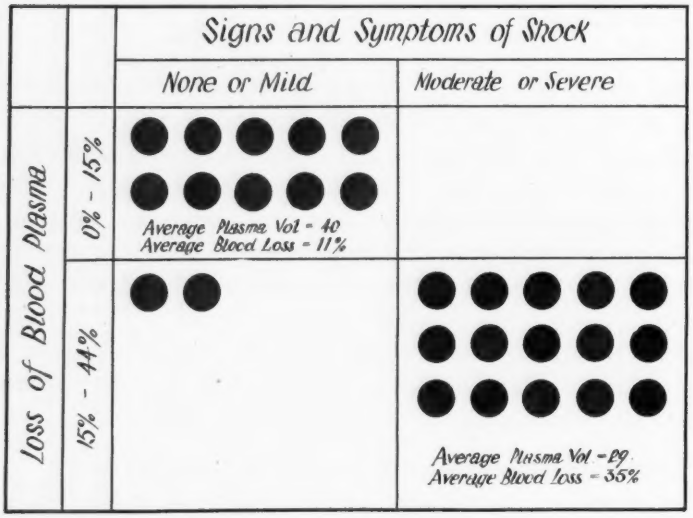

CHART 3.—Scattergram showing the relation of blood loss to severity of shock in simple acute blood loss.

patients who suffered any of the following fractures: Fractures, simple or compound, of the pelvis, femur, or tibia and fibula. The *abdominal injuries* consisted mainly of gunshot or stab wounds (perforating) of the abdominal cavity; also included are several patients with traumatic rupture of the small intestine. The *chest injury* group included all stab and gunshot wounds of the thorax, along with those patients with crushing injuries of the chest. The shock picture in this group is complicated many times by coexisting pneumothorax.

In Tables I, II, III and IV have been placed much of the collected data on this large group of 143 patients who have suffered traumatic injury. Space does not allow for an inclusion in these tables of all the clinical

TABLE III

CHEST INJURY

Shock—None or Mild

Patient	Diagnosis	B.P.	Pulse Rate	Pulse Quality	Venous Filling	Extremities Temp.	Extremities Sweat.	Plasma Volume	Hemato-crit	Plasma Protein
M. P.	Stab wound, hemothorax	88/58 to 120/70	102	Good	Good	Warm	Dry	41	37	5.9
G. B.	Stab wound	90/70 to 110/80	78	Good	Fair	Warm	Dry	44	33	6.7
M. P.	Bullet wound, hemothorax	132/80	80	Good	Good	Warm	Dry	38	35	6.5
A. H.	Bullet wound, chest	130/68	90	Good	Good	Warm	Dry	38	40	?
N. L.	Stab wound, hemothorax	80/60	92	Fair	Fair	Cold	Dry	38	39	?
J. B.	Stab wound	90/70 to 110/70	120	Fair	Fair	Warm	Dry	40	44	7.2
J. M.	Stab wound	90/60	120	Fair	Poor	Warm	Moderate	35	36	5.4
B. G.	Bullet wound	120/80	80	Good	Good	Warm	Dry	38	40	6.2
		Shock—Moderate or Severe								
C. G.	Stab wound, hemothorax	80/60	98	Good	Fair	Warm	Dry	29	43	7.0
B. B.	Stab wound, hemopneumothorax	60/20	88	Fair	Good	Warm	Marked	29	43	?
L. P.	Bullet wound, hemopneumothorax	50/28 to 80/58	96	Poor	Fair	Cold	Marked	29	43	6.1
W. C.	Stab wound, hemopneumothorax	60/40	95	Fair	Fair	Warm	Marked	33	44	5.7
*H. S.	Multiple rib fractures, axillary vein rupture	165/100 to 70/50	108	Fair	Poor	Cold	Marked	31	37	6.5
E. G.	Stab wound, hemopneumothorax	65/45	100	Poor	Poor	Warm	Marked	26	44	6.7
R. W.	Gunshot wound, chest and abdomen	50/?	160	Poor	Poor	Cold	Marked	31	45	6.8
D. F.	Crushed chest	110/80 to 70/50	70	Good	Fair	Cold	Dry	22	46	6.9
I. P.	Crushed chest	50/0	84	Poor	?	Cold	Dry	25	46	7.8
E. B.	Multiple fract., ribs	70/50	72	Poor	?	Cold	Dry	31	46	6.7
E. H.	Bullet wound, hemothorax	50/20	130	Poor	Fair	Warm	Dry	27	39	6.2
J. C.	Bullet wound, hemopneumothorax	70/40	128	Poor	Fair	Cold	Dry	26	36	5.8
E. W.	Stab wound, hemothorax	50/? to 80/60	120-102	?	?	Cold	Marked	29	49	7.0
W. R.	Shotgun wound, cardiac tamponade	60/40	96	Poor	Good	Cold	Marked	42	45	7.0
L. H.	Stab wound, hemothorax	Unobt.	73	Very poor	Fair	Cold	Dry	26	..	...
J. E.	Fract. ribs, massive hemothorax	40/?	150	Poor	Poor	Cold	Marked	25	45	?
E. M.	Bullet wound, aorta & heart, massive hemothorax	60/40	110	Poor	Poor	Cold	Marked	25	43	7.2
J. F.	Fract. of 5 ribs, hemopneumothorax	75/45	76	Poor	?	Cold	Dry	28	39	?
R. W.	Bullet wound, hemopneumothorax	50/?	160	Poor	Fair	Cold	Dry	32	44	6.8
W. J.	Stab wound, sucking pneumohemothorax	70/50	90	Fair	Fair	Warm	Dry	31	41	7.4
W. B.	Stab wound, hemopneumothorax	60/40	88	Poor	?	Cold	Marked	39	36	6.0
J. B.	Bullet wound, internal mammary artery	unobt.	100	Poor	Poor	Cold	Marked	20	44	6.9
*C. A.	Fract. sternum, contusion of heart	60/40	63	Poor	Good	Cool	Dry	45	44	7.2
H. F.	Contusion of heart	60/30	65	Poor	Poor	Cool	Dry	45	44	7.2
S. B.	Stab wound, internal mammary artery	65/45	68	Poor	Poor	Warm	Dry	28	43	6.9

data collected on the individuals of this group. The great majority of the patients were young or middle aged, and colored. References can be made to these tables for the pertinent shock data on these patients, such as early clinical signs of shock (which will be discussed below), plasma volume, hematocrit, and total plasma protein in per cent.

I. *Plasma Volume* in Acute Blood Loss.*—For purposes of ready analysis, plasma volume data on the individual groups have been arranged in scatter-

CHART 4
Skeletal Injury

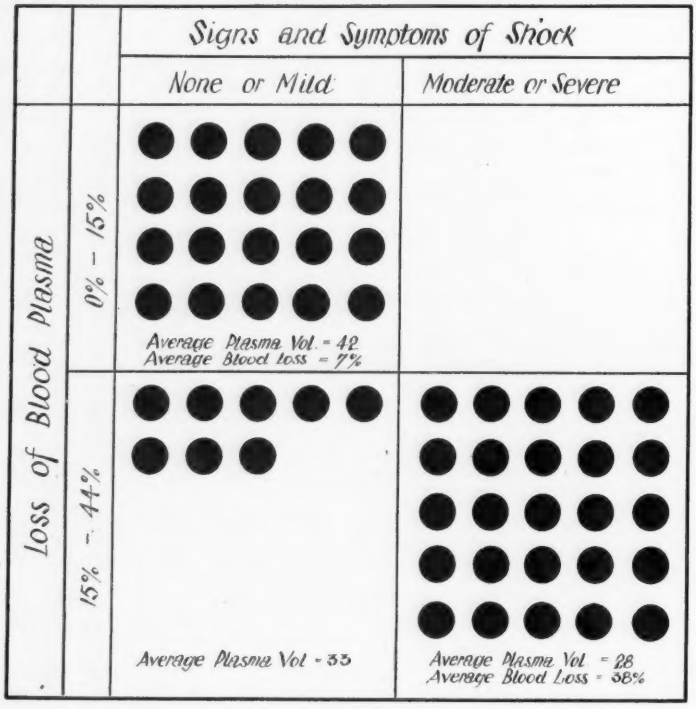

CHART 4.—Scattergram showing the relation of blood loss to the severity of shock in skeletal trauma.

gram fashion. In Chart 3 it will be seen that in the patients with acute blood loss in whom shock was absent, or only mild, the average plasma volume was 40 cc. Kg., representing an average blood loss of only 11 per cent. In the acute blood loss group where shock was moderate or severe, the average plasma volume was 29 cc. Kg., representing an average blood loss of 35 per cent.

II. *Plasma Volume in Skeletal Trauma.*—In the scattergram shown in Chart 4 that group of the skeletal trauma patients who showed no, or only

* We have accepted 45 cc. Kg. as the normal figure for plasma volume for adults. (Gregersen, and our unpublished data)

TABLE IV

ABDOMINAL INJURIES

Shock—None or Mild

Patient	Diagnosis	B.P.	Pulse Rate	Pulse Quality	Venous Filling	Extremities Temp.	Extremities Sweat.	Plasma Volume	Hemato-crit	Plasma Protein
J. M.	Gunshot wound	90/70	120	Fair	Good	Warm	Mild	39	44	6.0
J. K.	Gunshot wound	95/60 to 110/70	80	Good	Good	Warm	Dry	32	46	7.0
M. A.	Gunshot wound	130/70	90	Good	Good	Warm	Dry	38	..	...
S. P.	Gunshot wound	140/100	90	Good	Good	Warm	Dry	43	45	7.0
L. T.	Stab wound	128/80	114	Good	Good	Warm	Dry	39	43	6.2
E. G.	Gunshot wound	105/70 to 90/60	78	Good	Good	Cold	Dry	38	40	6.2
J. B.	Gunshot wound	132/90	96	Good	Good	Warm	Dry	43	54	7.2
B. A.	Gunshot wound	110/85	75	Good	Good	Warm	Dry	39	41	6.8
S. R.	Gunshot wound	120/80	80	Good	Good	Warm	Dry	35	48	6.2
L. F.	Gunshot wound	124/84	123	Good	Good	Warm	Dry	43	43	6.8
D. G.	Stab wound of liver	120/80 to 80/60	100	Fair	Good	Warm	Dry	39	43	6.8
E. P.	Gunshot wound	130/80	98	Good	Good	Warm	Dry	46	44	6.9
A. M.	Stab wound, late periton...	130/70	98	Good	Good	Warm	Dry	24	31	6.3
J. T.	Gunshot wound	140/100	95	Fair	Poor	Warm	Dry	28	49	6.4

Shock—Moderate or Severe

W. S.	Gunshot wound	84/60 to 64/35	120	Fair	Good	Warm	Dry	32	44	6.2
O. H.	Ruptured ileum (traumatic)	60/40	100	Poor	Fair	Warm	Dry	24	55	5.6
M. T.	Gunshot wound	60/40	95	Fair	Fair	Cool	Dry	28	43	6.8
A. M.	Rupt. jejunum (traumatic)	75/50	120	Poor	Poor	Cold	Marked	22	51	7.2
R. J.	Stab wound, liver	50/35	100	Poor	Poor	Cold	Dry	28	38	5.9
C. H.	Rupt. bladder, peritonitis	140/120	155	Poor	Poor	Cool	Dry	25	57	?
M. J.	Stab wound	50/0	140	Poor	Poor	Cold	Marked	25	37	5.6
W. W.	Rupt. jejunum (traumatic)	90/40	160	Poor	Poor	Cold	Marked	18	60	7.3
H. G.	Gunshot wound	110/70 to 70/50	120	Poor	Poor	Cold	Dry	32	40	?
J. M.	Stab wound	120/80 to 60/40	100	Good	Good	Warm	Dry	34	41	6.9
G. M.	Peritonitis	Unobt.	Unobt.	Unobt.	Poor	Cold	Marked	25	44	5.5
A. C.	Stab wound	80/50	84	Good	Good	Warm	Moderate	32	45	7.2
M. B.	Rupt. uterus	130/70 to 60/30	78	Good	Good	Warm	Dry	29	32	6.0
L. A.	Gunshot wound	70/50	88	Fair	Fair	Warm	Mild	31	40	5.8
L. S.	Stab wound	84/45	70	Fair	Good	Cool	Dry	32	27	7.0
J. M.	Stab wound	105/70 to 80/60	96	Good	Good	Cold	Marked	30	36	5.8

mild, signs of clinical shock have an average plasma volume of 42 cc. Kg., which represents an average blood loss of only 7 per cent. On the other hand, in those skeletal trauma patients in whom shock was moderate or severe, the average plasma volume was 28 cc. Kg., which represents an average blood loss of 38 per cent.

III. *Plasma Volume in Abdominal Injuries.*—In the scattergram shown in Chart 5 it will be noted that the plasma volume of the "none or mild" shock group is 42 cc. Kg., representing an average blood loss of only 7 per cent, while in the moderate or severe group, the average plasma volume is 28 cc. Kg., or a represented blood loss of 38 per cent.

IV. *Plasma Volume in Chest Injuries.*—The study of shock in chest injuries is complicated by at least three important factors, other than blood

loss. Patients may receive heart wounds such that little or no external or internal blood loss occurs, but cardiac tamponade results. Secondly, direct trauma over the precordium may result in cardiac contusion, from which shock may result. Thirdly, the presence of a large pneumothorax, open or closed, complicates and makes more severe any shock, especially when the attendant large blood loss is great.

It will be seen (see Chart 6), therefore, that patients in the chest injury group showing little or no signs of shock have an average plasma volume of 40 cc. Kg., which represents a blood loss of only 11 per cent, while in the group showing signs of moderate or severe shock, there are two patients

CHART 5
Abdominal Wounds

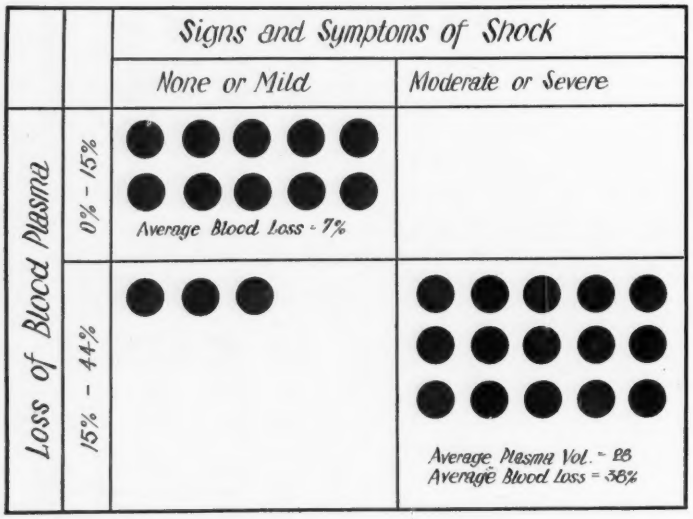

CHART 5.—Scattergram showing the relation of blood loss to the severity of shock in abdominal wounds.

with cardiac tamponade, and two with cardiac contusion, who lost very little blood. However, in all chest injury patients in whom blood loss was a real factor in the production on shock, the average plasma volume was 28 cc. Kg., which represents a blood loss of 38 per cent.

WHAT IS LOST FROM THE BLOOD STREAM IN SHOCK?

Chart 7 represents a diagram of the hematocrit values of these patients. A study of this chart will indicate to the reader that, in the main, the hematocrit values (the average of 3–6 individual readings taken during the plasma volume determination) show little evidence of hemoconcentration. Hence, it is readily evident that what is lost from the blood stream early in shock as a result of trauma must be *whole blood* and not its liquid component,

plasma. The protein figures (to be found for the individual patient in Tables I–V) indicate that if dilution of the blood is taking place by drawing in of fluids from the extravascular spaces to compensate for blood loss, the diluting fluid must closely simulate plasma.

Because of the hematocrit values obtained in this study, we believe we are justified in calculating from our plasma volume data an estimate of whole blood loss which, as has been seen in the various groups of shock

CHART 6
Chest Injury

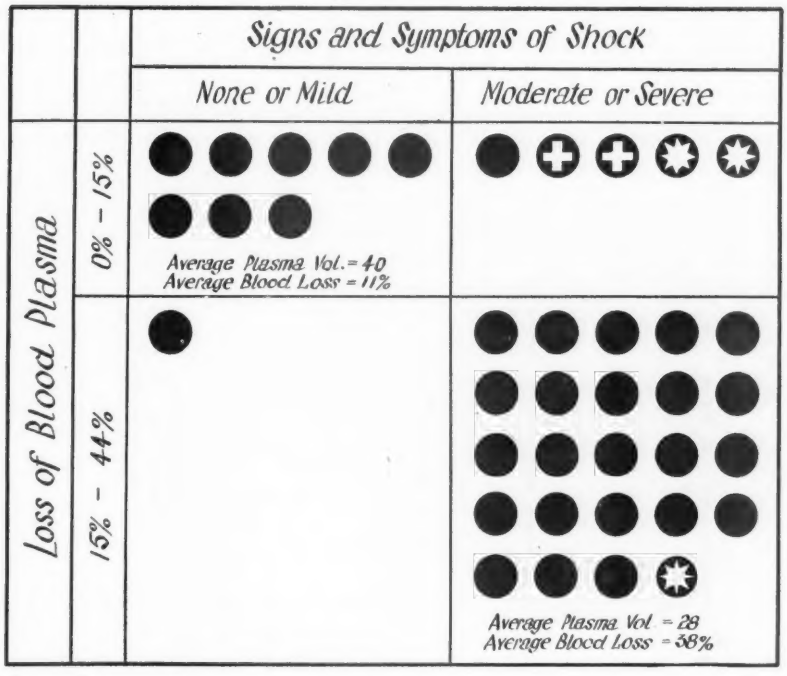

CHART 6.—Scattergram showing the relation of blood loss to the severity of shock in chest injuries.

patients studied, is for the "moderate and severe" groups, 35 per cent, 38 per cent, 38 per cent and 38 per cent, respectively.

It will be noted in Charts 3–6 that several patients, especially in the skeletal trauma group, showed no, or only mild, signs of shock even though the blood loss was greater than 15 per cent. In these patients it is evident that physiologic adjustment to blood loss (other than fluid replacement to the vascular system) was rapidly made. It is noteworthy, however, that only one patient of the entire series (in the chest injury group) showed signs of moderate or severe shock with a blood loss of less than 15 per cent.

In the abdominal injury group, it will be noted on Chart 7, that five patients

had hematocrit readings above 50 per cent. Reference to Table III will show that four of these patients had a ruptured viscus (three—ruptured small bowel; one—bladder). These studies suggest that if a patient is seen in shock with a gunshot wound of the abdomen and the hematocrit value is above 50, the chances are fair that there has been a perforation of a viscus, with peritonitis resulting.

THE EARLY CLINICAL SIGNS OF TRAUMATIC SHOCK

Because of the relative scarcity of information on the *early* clinical signs of shock we have endeavored to collect observations on these points.

(a) *Blood Pressure Readings.*—Blood pressure readings were made on the arm, using a pneumatic cuff and a standardized mercury manometer. At least three or four readings were made during the hour—sometimes more. It is emphasized that these readings are made with the patient in the moderate Trendelenburg head-down position (usually about 15°).

CHART 7

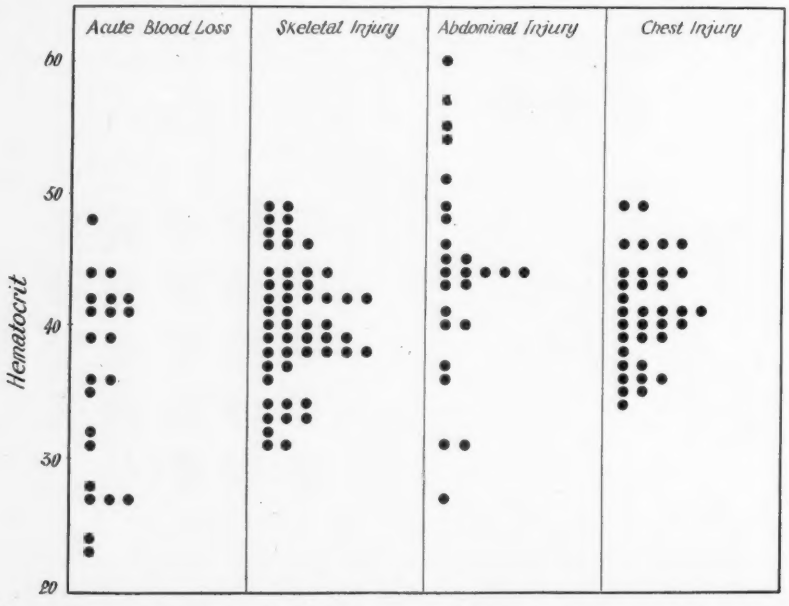

CHART 7.—Scattergram showing the average hematocrit readings in clinical shock produced by acute blood loss, skeletal trauma, abdominal wounds, and chest injuries. Except for the five patients in the abdominal injury group (mentioned in text), there is no indication of hemoconcentration early in the shock state. This suggests the loss of whole blood, rather than plasma alone, early in the shock state.

(b) *Pulse Rate and Pulse Quality.*—Pulse rate and quality were recorded from the radial pulse and usually checked (rate) at the precordium.

(c) *Venous Filling Time.*—This simple test, as employed by us, consists of emptying by pressure stroking of the finger one or more of the visible veins in the outstretched, ventral surface of the forearm and noting the time taken by the vein to refill. Although this is admittedly a crude indicator of peripheral blood flow to an extremity, this test has, at times, given us valuable information as to the severity of shock present, especially in

CHART 8
Acute Blood Loss

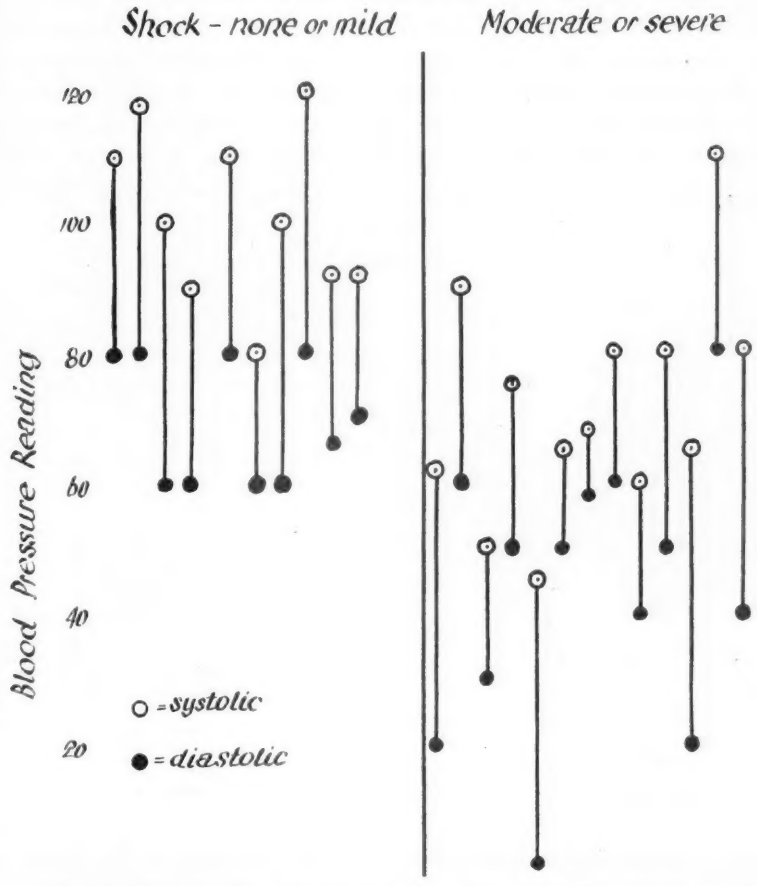

CHART 8.—Diagram illustrating the relation of blood pressure readings to the severity of shock in acute blood loss.

those individuals in whom we have found an initially relatively normal blood pressure but which was found later to be falling.

(d) *Sweating and Temperature of the Extremities.*—The sign of cold, clammy extremities has been accepted by many as being almost always present in shock, so we were interested in making observations on how soon this sign appeared and how well its presence or absence correlated with the blood volume estimation. No attempts were made to record temperature accurately; we simply tried to estimate, in a clinical fashion, whether the hands and feet were warm, cool or cold, and whether they were wet with perspiration or dry.

These are, in general, simple clinical tests that can be applied in the field and which, except in the case of blood pressure readings, employ no special apparatus.

BLOOD PRESSURE IN SHOCK

In Charts 8–11 the blood pressure readings for each group have been

placed together, according to the degree of shock manifested on clinical examination. The data on the blood pressure readings in relation to the severity of shock seem to justify the opinion that, no matter what the injury causing the shock, there is a fairly good correlation between the severity of shock and blood pressure readings. By reference to Tables I to IV, the reader will note that in most cases where the blood pressure was found to be relatively low the patient showed clinical signs of severe shock, *i.e.*, cold, wet extremities, *etc.* We have not tried to work out a correlation between

CHART 9

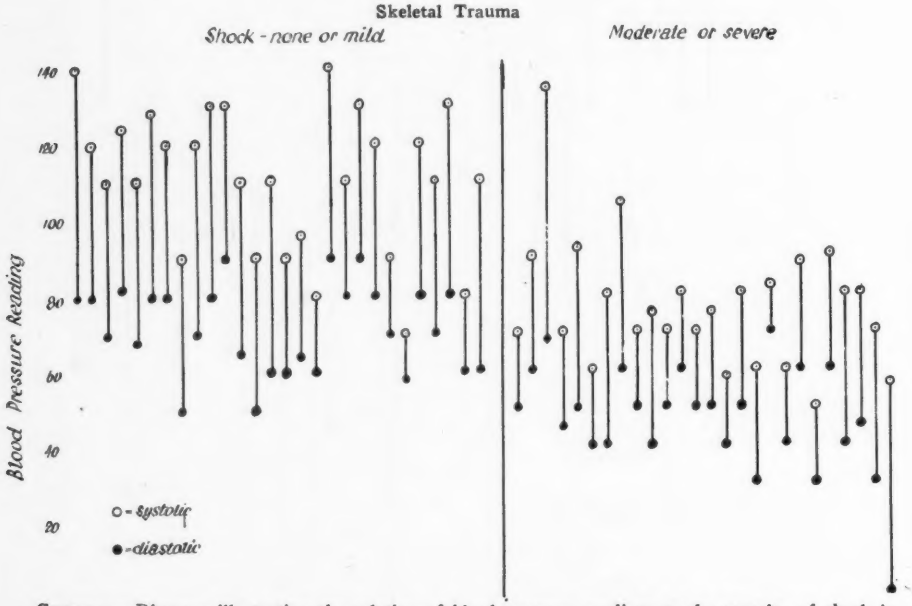

CHART 9.—Diagram illustrating the relation of blood pressure readings to the severity of shock in skeletal trauma.

the blood pressure readings and the degree of reduction of blood volume but it is readily evident from a study of the data in Tables I to IV that only rarely does one find a persistent low blood pressure when there has been little or no blood loss. Indeed, in most patients studied in this series there is a good correlation between the degree of reduction of blood volume and blood pressure readings.

Keith[2] found that cases of wound shock fell into three groups: Group 1. The *compensated* cases in which there was very little blood loss, the blood pressure tending to remain above 100 mm. mercury. In Group 2, the *partially compensated* cases, the blood loss was between 25 per cent and 35 per cent. In these cases the systolic blood pressure was usually between 70 and 80 mm. mercury and a rapid pulse was found. In Group 3, *uncompensated* cases, the blood volume reduction was greater than 35 per cent, and these patients had generally a systolic blood pressure around 60 mm. mercury, with a very rapid heart rate.

The relations between low blood pressure and reduced blood volume,

CHART 10

Abdominal Injuries

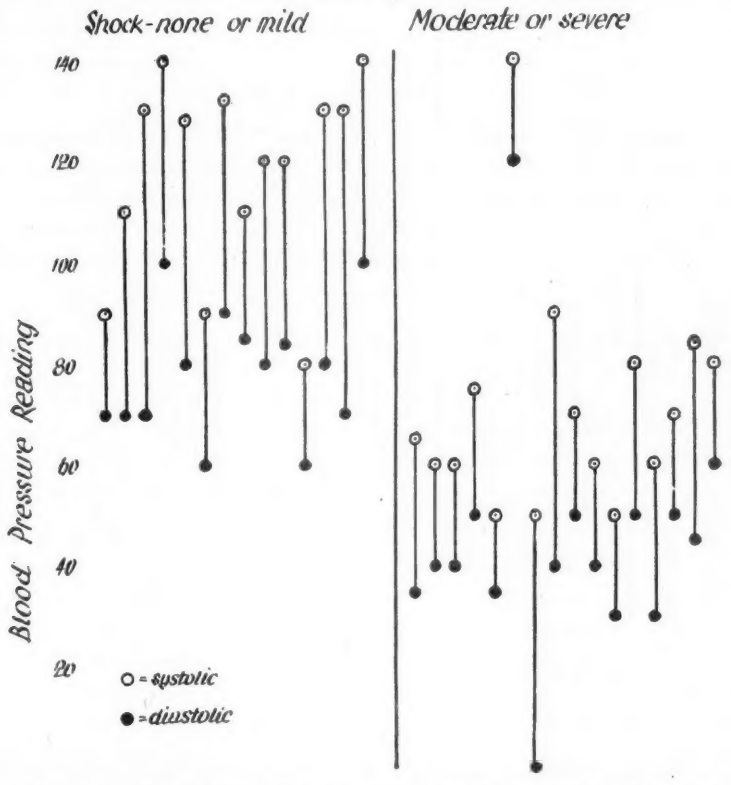

CHART 10.—Diagram illustrating the relation of blood pressure readings to the severity of shock in abdominal injuries.

reported by Keith, correspond to estimates that we have made with improved blood volume methods. An examination of our data leads us to the conclusion that if a patient has received trauma of the types studied by us and the blood pressure tends to remain below 90 mm. systolic, the chances are very great that there has been a considerable blood loss. If, on the other hand, the patient has received severe trauma and, in the Trendelenburg position, maintains a systolic blood pressure above 90 mm. mercury it is probable that he has either suffered little blood loss or has rapidly compensated by blood volume restoration for the amount of blood lost.

In this study, therefore, the blood pressure readings have given us a valuable index as to the severity of blood loss in traumatic shock and the degree of reduction of blood volume. This, likewise, was the conclusion of Kewick, *et al.*,[13] who studied 24 cases of secondary traumatic shock during the bombing of London in 1940.

We have not been impressed with the value of the pulse rate as an index of severe traumatic shock. Reference to Tables I to IV will show that there have been many cases where the blood pressure has been found to be at shock levels, the plasma volume estimation indicating a serious deple-

CHART 11
Chest Injuries

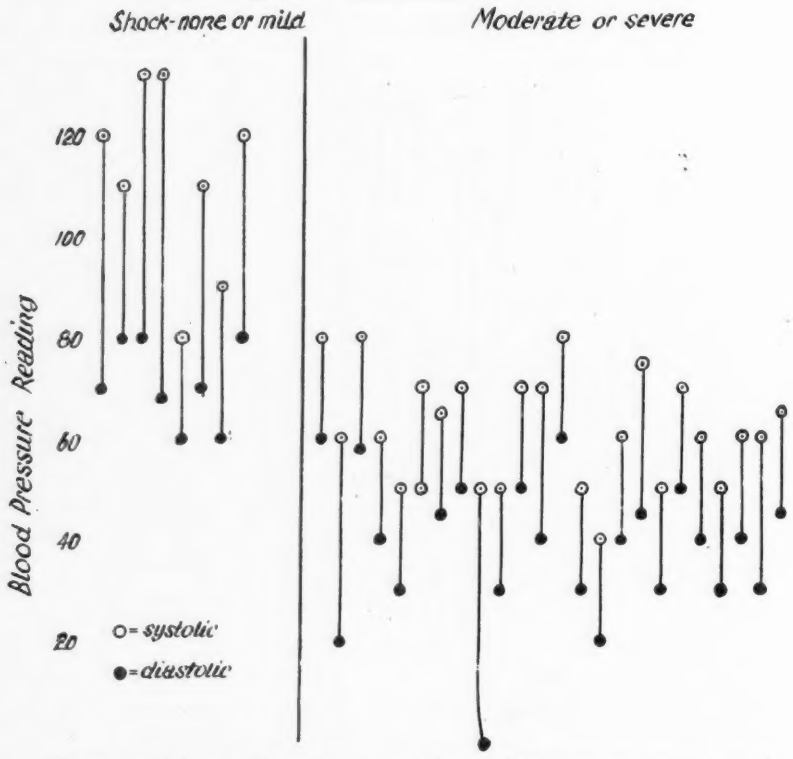

CHART 11.—Diagram illustrating the relation of blood pressure readings to the severity of shock in chest injuries.

tion of blood volume, while the pulse rate remained more or less within the normal range. We have seen no evidence in our study to indicate that in severe trauma a slow pulse necessarily indicates severe shock. In shock cases seen shortly after the trauma has been received, it is not at all uncommon to find a relatively slow pulse; this is especially true in severe chest injuries.

In individual shock cases an estimation of venous filling time has at times given us a valuable index as to the severity of shock. A study of this point in Tables I to IV indicates that in patients who have received severe trauma but who show little or no signs of shock, the venous filling time is within normal limits, whereas in those patients who have received severe trauma and show evidence of moderate or severe shock, the venous filling time may be considerably prolonged.

Likewise, when venous filling time has been found to be greatly retarded, the temperature of the extremities has been found to be considerably lowered from the normal. It was surprising to us, however, to find that in many patients in severe shock there was relatively little sweating of the extremities, so that we are under the impression that the temperature of the extremities is a far more important indicator of shock than whether or not sweating is present. Indeed, very often one finds in severe shock a cool or cold

extremity which remai..s dry. Dehydration may have been a factor in our series but we are inclined to doubt this because our patients were seen so soon after the trauma had been received.

PATCHY CYANOSIS

During this study we have had the opportunity to observe six patients who have suffered extreme trauma and who have exhibited the phenomenon that we have termed "patchy cyanosis." The picture may be described briefly as small areas of cyanosis (usually 1 to 2 cm. in diameter) scattered closely together on a background of pale, extremely ischemic skin. The phenomenon was seen best on the anterior chest and abdomen. The areas of patchy cyanosis resemble in some respects Bier's spots, except that they are larger and are on a background of ischemic skin. There appeared to be no tendency for these areas of cyanosis to coalesce.

In some regards these areas resemble the patchy ischemia produced in experimental animals by rapid depletion of blood volume, studied so extensively by Rous and Gilding.[14]

Our reason for calling attention to this sign is that, in our experience, its appearance in patients who have suffered severe trauma has portended in all cases, with the exception of one, an early fatal outcome. In one patient large amounts of blood and plasma were given rapidly; this and other signs of shock then disappeared, with the blood pressure assuming more normal levels. The patient died 48 hours later of an associated cerebral lesion. In the other five patients blood and plasma infusions were started soon after the patients were first seen but death ensued before any considerable increase of blood volume could be effected.

It is our impression that if this sign is seen in shock patients every effort should be made to restore blood volume as rapidly as possible. Even so, the outcome will likely be fatal.

EARLY HEMOCONCENTRATION IN TRAUMATIC SHOCK

Ever since the appearance of Scudder's[15] book on shock, it has been thought by many that the determination of specific gravity of whole blood or plasma would give valuable information in the early diagnosis of shock or impending shock in the patient who has suffered trauma. Indeed, Scudder stated in the final summary of his book (page 195) that the weight of a drop of peripheral blood may serve as a measure of this hemoconcentration, and is of more value than blood pressure determinations, as it heralds, by many hours, its ultimate fall. Moon[16] stated: "Experience with this criterion (hemoconcentration) has led me to the conviction that hemoconcentration is the earliest detectable manifestation of shock, as well as the most accurate index of its severity."

We are inclined to believe that determinations of specific gravity of whole blood (or hematocrit determinations) may be of distinct value in following the clinical course of patients with abdominal wounds or other

states in which plasma loss may be profound. It is evident from the analysis of the hematocrit data presented in Chart 7 that the estimation of specific gravity of whole blood would be of little if any aid in the early diagnosis of traumatic shock simply because there is no evidence of hemoconcentration early in traumatic shock. Unfortunately, as this study shows, it is whole blood that is lost in the initial stages of clinical traumatic shock.

From this study of the early clinical signs of shock, we are, therefore, impressed mainly with the value of blood pressure readings. As has been brought out by other writers, the blood pressure reading may be within normal limits when the patient is first seen but if readings are taken every 10 to 15 minutes, in most patients in severe shock (who on blood volume determination will show a considerable decrease in blood volume) it will be found, generally, that the blood pressure readings tend to become lower and lower with the passage of time if treatment of shock is not instituted early. As our group has seen more and more shock patients we have learned that a trained observer can often estimate, with surprising accuracy, the plasma volume simply by taking into account the blood pressure level, the injury, and the state of the patient.

DISCUSSION

It would be unfair to convey the impression that the group of investigators associated with Cannon,[1] and Bayliss,[17] did not appreciate the importance of the depletion of blood volume as a factor in the causation of wound shock. The demonstration by Keith[2] that the shocked man had a seriously reduced blood volume, whether shock was due primarily to hemorrhage or to a combination of hemorrhage and trauma, seems to have been readily accepted. What is more important from a therapeutic standpoint, restoration of blood volume by transfusion of whole blood or gum acacia solution was early advanced as the most efficient method to treat shock. Keith stated definitely that "recovery from wound shock is associated with an increase in blood volume" (page 16). Nevertheless, the question still puzzled many—what was the cause of the reduction of blood volume in wound shock?" ("However, that the reduction of blood volume is secondary to some still unknown primary cause seems evident." [Keith, page 15]).

Although Cannon and Bayliss[18] were convinced of the importance of blood loss as a factor in the production of shock, they entertained strongly the possibility that "the injured muscle would produce metabolites which, on being absorbed into the blood stream, would indicate their presence by a decrease in the blood pressure, with other signs of shock" (page 21).

It is not necessary to go into a long consideration of the many conflicting views regarding the importance of traumatic toxemia as a significant factor in the production of shock, since the evidence has been weighed so carefully in the communications of Parsons and Phemister,[19] and more at length in the excellent treatise of Blalock.[20] As Blalock has pointed out, it is un-

fortunate that so many of the experimental studies which have been carried out to test the correctness of the traumatic theory bear little relation to the clinical problem of shock (the implantation of muscle, *etc.*, into the peritoneal cavity, ligation of muscle masses, intravenous infusion of tissue extracts). In his search for the truth concerning traumatic toxemia, the reader may become bewildered by some of the writings on this subject.

We wish to emphasize here that we have seen the signs of moderate or severe shock appear in patients who have suffered any of four rather different types of body injury, yet the degree of reduction of circulating blood volume in each of the groups was approximately the same. This would indicate to us that in all studies involving an attempt to identify certain toxins as a causative factor in traumatic shock this common factor of blood loss, no matter what the injury, should be properly evaluated.

Certain recent studies have indicated the importance of the decrease in cardiac output as an initiating factor in the production of shock. We are inclined to the view from an analysis of our clinical shock material to believe that in clinical traumatic shock this follows an early reduction in blood volume, soon after the injury has been received. This is more evident in patients who have suffered lacerations of arteries or veins or stab and gunshot wounds of the chest and abdomen. Undoubtedly, in many patients there is a primary fall in blood pressure due to neurogenic causes.

In experimental studies, as Blalock and others have shown, it is possible to show that the decrease in cardiac output precedes a decrease in blood pressure levels. In clinical practice, however, it is our opinion that by the time most patients can be seen after severe trauma has been received, the blood pressure will have fallen to shock levels. From then on both cardiac output and blood volume remain low until efforts are made to restore blood volume by plasma or blood infusions. If restoration of blood volume and return of cardiac output to fairly normal levels cannot be effected, the patient passes more or less rapidly into generalized anoxia, in which state all the capillary walls become affected. When this stage is reached, as clinical experience has shown, blood or plasma infusions are no longer effective.

In our attempt to determine the most important factors in the cause of shock, we have not felt the need to consider toxemia as an initiating or contributing factor. Likewise, there has been no occasion to consider dehydration or exposure to cold as contributing factors since our patients in general were seen shortly after reception of the trauma.

The careful reader cannot fail to be impressed with three factors acting in the production of shock observed in wounded soldiers by Cannon, Bayliss, Robertson, Keith, and others during World War I. Their subjects were in the main (1) cold from exposure to wet, cold atmosphere; (2) apparently dehydrated; and (3) a long time getting back to a point "behind the lines" where shock could be treated properly. Should an active military campaign be pursued again in climates similar to that found in Flanders, exposure to

cold and rain should not be relegated to the background as a possible important factor in the causation of wound shock.

In conclusion, we wish to state that although we regard extreme blood loss at the site of injury as the most important single factor in the causation of traumatic shock, there is no evidence in our observations to exclude the possibility that toxic metabolites absorbed from the zone of injury in severe muscle trauma are not in part responsible for some of the shock picture. This would be especially probable should there be an associated infection in the wound and the patient is seen late. Further, in severe crushing chest injuries where the signs of shock come on rapidly and the patient responds poorly to intravenous infusion of large amounts of blood and plasma, we believe that some cause other than blood loss is responsible for the early fatal outcome in these patients. Indeed, in this group it would appear that there is a rapid and extreme disarrangement of the whole body mechanism. In this group we are inclined to consider seriously a neurogenic factor as being important in the production of shock.

SUMMARY

Using the Gregersen-Gibson method for the estimation of plasma volume in patients who have experienced various types of trauma, it has been found that signs of severe shock do not ordinarily appear unless the blood loss is greater than 15 per cent. The average blood loss in severe traumatic shock has been about 38 per cent, no matter what the nature of the trauma. From analysis of dye disappearance curves, we have found no evidence of increased generalized capillary permeability in traumatic shock. From hematocrit studies, it is evident that what is lost early in traumatic shock in the zone of injury is whole blood, not plasma.

Severe depletion of blood volume appears to be the most important single factor in the causation of traumatic shock.

A decline in blood pressure levels appears to be the most valuable clinical sign in the early diagnosis of clinical shock.

We wish to express our gratitude to our chief, Dr. I. A. Bigger, for arranging the facilities that made these clinical studies possible.

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LIPOSARCOMA—THE MALIGNANT TUMOR OF LIPOBLASTS*

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SURELY, one of the most bizarre and fantastic chapters in the story of oncology is furnished by the tumors of fat-forming cells. The strange way in which they grow, their astounding size, equalled by no other tumor, and many other peculiar features and relationships make them of great interest. A good deal of information exists about benign fatty tumors but not nearly as much is known about the malignant ones because of their rarity. For this reason it seems worth while to record the group of 41 cases of liposarcoma which have gradually accumulated in the Laboratory of Surgical Pathology of Columbia University during the past 37 years, and to integrate the information gained from them with what can be gleaned from the publications of others.

As Gideon Wells has so ably pointed out in his fascinating review, adipose tissue has been sadly neglected and fat, which is certainly a substance known to everyone, has been the subject of extraordinarily little scientific investigation. Even its histogenesis is in doubt. Wells discusses this question and the majority of modern observers will agree with him that the older conception of the fat cell as a modified fibroblast (Jacobsen) which has assumed the function of fat storage is no longer tenable. According to Hausberger, Chlopin and Burkhardt the lipoblast is a specialized cell differing from the fibroblast although derived like it from vascular mesenchyme. This difference is emphasized when the lipoblasts of a liposarcoma are grown *in vitro*. Murray and Stout have shown that they can readily be distinguished from fibroblasts. Wells is inclined to accept the work of Wassermann who derives the fat organs from special perivascular mesenchymal cells supposedly related to reticulum and thus makes fat a close relative of lymphoid tissue and the reticulo-endothelial system. Wells supports this by citing the well known interrelationships of fat and lymphoid cells in lymph nodes and thymus and the occasional finding of extramedullary hemopoiesis in fat. But such an assumption does not take into account all of the facts demonstrated by tumors. There are many lipomas, especially the deep intramuscular variety, which are not only associated with blood vessels so that in some areas they look like pure hemangiomas but also with the formation of masses of smooth muscle and there are liposarcomas in which well differentiated bone is a prominent feature (Knox; Josephson and Westberg; Dreyfuss and Lubash; Case 40). Moreover Babès found normoblasts, megakaryocytes and plasma cells in one liposarcoma reported by him. Thus,

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it seems safer to regard the lipoblast as an ordinarily specialized fat-forming mesenchymal cell which on occasion can produce a very wide variety of different and complex tissues.

Although lipomas are very common tumors; malignant fat tumors are rare. Moreland and McNamara found only nine liposarcomas among 16,000 tumors of all kinds. In the laboratories of pathology and surgical pathology of the Presbyterian Hospital there are recorded 1454 lipomas and 21 cases of liposarcoma. Since many patients with lipomas never have them removed, the incidence is probably even less frequent.

Perhaps the most sensational feature of fatty tumors is the enormous size which they may attain. Wells says that he has seen a case of liposarcoma which weighed 69 pounds (32 kilos). Other tremendous liposarcomas, are recorded by McConnell (65 lbs.), Salzer (63.8 lbs.), Vanderveer (56 lbs.), Williams (51 lbs.), Harrington (47 lbs.), Madelung (38.5 lbs.), Waldeyer (30 lbs.) and Wechsler (25 lbs.). These massive tumors were all either mesenteric or retroperitoneal, with a predilection for the perirenal zone. The record weight and size for a tumor of any kind, so far as I am aware, is held by Delamater's case. This was a fatty tumor which was retroperitoneal and protruded posteriorly outside the left labium majus and buttock so as to form a mass four feet in circumference while the circumference of the abdomen was seven feet eight inches. When she was weighed about three years before her death she registered 269 pounds, of which it was estimated that 179 pounds were tumor. Supposing that the tumor continued to grow at the same rate of speed after weighing as before, Delamater reckoned that the tumor weighed 275 pounds at death. Even if one rejects this second figure, a tumor weighing 179 pounds dwarfs any of the more recently recorded cases. Delamater's account of this woman's life history from the age of 25, when the abdominal mass was first palpated, until her death in her 36th year is detailed and most interesting, for after a preliminary period of discomfort she became adjusted to the huge mass and, except for its weight which kept her bedridden for the last four years, breathed freely, ate well with good appetite, menstruated regularly, evacuated her bowels easily and remained cheerful. Most extraordinary of all she became pregnant five years before death, although the fetus was born dead (Fig. 1).

FIG. 1.—Enormous retroperitoneal lipoma weighing at least 179 pounds and possibly 275 pounds. (Reproduced from Delamater's paper in the Cleveland Medical Gazette.)

Adair, Pack and Farrior state that lipomas are more common in females (73 per cent). This sex discrepancy does not apply to liposarcomas, for in

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As Gideon Wells has so ably pointed out in his fascinating review, adipose tissue has been sadly neglected and fat, which is certainly a substance known to everyone, has been the subject of extraordinarily little scientific investigation. Even its histogenesis is in doubt. Wells discusses this question and the majority of modern observers will agree with him that the older conception of the fat cell as a modified fibroblast (Jacobsen) which has assumed the function of fat storage is no longer tenable. According to Hausberger, Chlopin and Burkhardt the lipoblast is a specialized cell differing from the fibroblast although derived like it from vascular mesenchyme. This difference is emphasized when the lipoblasts of a liposarcoma are grown *in vitro*. Murray and Stout have shown that they can readily be distinguished from fibroblasts. Wells is inclined to accept the work of Wassermann who derives the fat organs from special perivascular mesenchymal cells supposedly related to reticulum and thus makes fat a close relative of lymphoid tissue and the reticulo-endothelial system. Wells supports this by citing the well known interrelationships of fat and lymphoid cells in lymph nodes and thymus and the occasional finding of extramedullary hemopoiesis in fat. But such an assumption does not take into account all of the facts demonstrated by tumors. There are many lipomas, especially the deep intramuscular variety, which are not only associated with blood vessels so that in some areas they look like pure hemangiomas but also with the formation of masses of smooth muscle and there are liposarcomas in which well differentiated bone is a prominent feature (Knox; Josephson and Westberg; Dreyfuss and Lubash; Case 40). Moreover Babès found normoblasts, megakaryocytes and plasma cells in one liposarcoma reported by him. Thus,

* Submitted for publication October 1, 1943.

it seems safer to regard the lipoblast as an ordinarily specialized fat-forming mesenchymal cell which on occasion can produce a very wide variety of different and complex tissues.

Although lipomas are very common tumors; malignant fat tumors are rare. Moreland and McNamara found only nine liposarcomas among 16,000 tumors of all kinds. In the laboratories of pathology and surgical pathology of the Presbyterian Hospital there are recorded 1454 lipomas and 21 cases of liposarcoma. Since many patients with lipomas never have them removed, the incidence is probably even less frequent.

Perhaps the most sensational feature of fatty tumors is the enormous size which they may attain. Wells says that he has seen a case of liposarcoma which weighed 69 pounds (32 kilos). Other tremendous liposarcomas, are recorded by McConnell (65 lbs.), Salzer (63.8 lbs.), Vanderveer (56 lbs.), Williams (51 lbs.), Harrington (47 lbs.), Madelung (38.5 lbs.), Waldeyer (30 lbs.) and Wechsler (25 lbs.). These massive tumors were all either mesenteric or retroperitoneal, with a predilection for the perirenal zone. The record weight and size for a tumor of any kind, so far as I am aware, is held by Delamater's case. This was a fatty tumor which was retroperitoneal and protruded posteriorly outside the left labium majus and buttock so as to form a mass four feet in circumference while the circumference of the abdomen was seven feet eight inches. When she was weighed about three years before her death she registered 269 pounds, of which it was estimated that 179 pounds were tumor. Supposing that the tumor continued to grow at the same rate of speed after weighing as before, Delamater reckoned that the tumor weighed 275 pounds at death. Even if one rejects this second figure, a tumor weighing 179 pounds dwarfs any of the more recently recorded cases. Delamater's account of this woman's life history from the age of 25, when the abdominal mass was first palpated, until her death in her 36th year is detailed and most interesting, for after a preliminary period of discomfort she became adjusted to the huge mass and, except for its weight which kept her bedridden for the last four years, breathed freely, ate well with good appetite, menstruated regularly, evacuated her bowels easily and remained cheerful. Most extraordinary of all she became pregnant five years before death, although the fetus was born dead (Fig. 1).

FIG. 1.—Enormous retroperitoneal lipoma weighing at least 179 pounds and possibly 275 pounds. (Reproduced from Delamater's paper in the Cleveland Medical Gazette.)

Adair, Pack and Farrior state that lipomas are more common in females (73 per cent). This sex discrepancy does not apply to liposarcomas, for in

39 liposarcomas in our own series there were 23 males and 16 females, while of 134 cases reported in the literature 71 were males and 63 females. Geographically, they are reported from Europe, Africa and the Americas. Cases from the Asiatic continent have not come to my attention.

The majority develop in the later years of life; 60 per cent of the Columbia University group were past 40 years when the tumor was first noticed, and the mean age was 53 years. Nevertheless, cases are reported in children. Fichman's case, which is somewhat questionable, was congenital, Kretschmer's case was 2 years old, Goeters' 2¾ years, Senftleben's 8 years, Sanes and Kenny's 16, while Pack and Anglem mention, without details, 13 cases under age 15. One must be prepared therefore to encounter the tumor at any age.

Trauma seems to play a very minor rôle in the etiology of this tumor. It preceded the appearance of the tumor in the thigh by three months in Jones and McClintock's case, and by a few days in Ackerman and Wheeler's second case, and accelerated the growth of a thigh tumor reported by Adair, Pack and Farrior. In Muller's case trauma to the back occurred one year before the appearance of a liposarcoma in the same locality. So far as our records show it did not play a rôle in any of the Columbia University cases.

There are certain regions of the body where liposarcomas are much more prone to develop than elsewhere. The retroperitoneal area and especially the perirenal portion of it, the mesentery and the omentum are most favored so far as cases previously reported are concerned, for nearly half come from these regions. It would seem, however, that this is due to selective reporting, for in the Columbia University group, which consists of 43 tumors in 41 patients only 7 (16.3 per cent) were in the retroperitoneal, perirenal, omental and mesenteric group. Far more common were the tumors arising in the thigh, popliteal space and gluteal region. There were 15 of these, or 35 per cent of the total. The other regions involved included the trunk 6, head, face and neck 5, inguinal canal and groin 3, leg 3, arm and forearm 3, and mammary gland 1. Other regions reported include intrathoracic (Ackerman and Wheeler; Barbier and Mollard, Chiovenda; Narr and Wells; Perkins and Bowers); meninges (Berger; Caldwell and Zinninger); spermatic cord (Kerschner; Dreyfuss and Lubash; Neal and Jolley; Marshall; Strong); bone (Barnard; Duffy and Stewart; Fender; Rehbock and Hauser; Stewart); vulva (Taussig; Kleeberg); common bile duct (Goeters); doubtful cases in the stomach by Abrams and Turberville, and in the uterus by Springer. Liposarcomas in animals are described by Haagensen and Krehbiel, and by Gavrilov and Silberfeld. Of the soft-part tumors a majority develop deeply from the inter- or intramuscular zones rather than from the subcutaneous fat where a majority of simple lipomas are located. Some tumors have been found closely attached to the sheaths of large blood vessels (Virchow 1857; Huet) but it seems very doubtful that they sprang from these sheaths. Equally open to question is the supposed relationship of lipomas and liposarcomas to nerves, inferred by Virchow 1857, Patel,

Adair, Pack and Farrior, and others. Wells discusses this question and wisely leaves it in abeyance. The development of lipomas is undoubtedly affected in some fashion by the nervous system but there exists no proof that malignant fatty tumors spring from nerve sheaths themselves.

Undoubtedly some liposarcomas develop from preexisting lipomas. This is stressed by Schiller, and Katz, and illustrated by our Case 21, where a definite liposarcoma was found completely surrounded by a simple retroperitoneal lipoma above the bladder. It is difficult to say how often it occurs because many of the tumors are composed of an intermingling of fully developed fat cells with neoplastic lipoblasts and one has no means of knowing whether or not this state of affairs existed from onset. It seems probable, however, that the large majority of malignant lipoblastic tumors are malignant from their beginning.

Wells discusses at some length the question of the availability of the lipoid in fatty tumors for use as a food in nutritional disturbances. He noted that the patient bearing the huge retroperitoneal liposarcoma, reported by Hirsch and himself, was emaciated to the maximum degree and yet the pounds of protein and fat it contained were not available to the patient. He quotes other cases of simple lipomas retaining their fat in wasting disease. None of the present group of liposarcomas demonstrated this peculiarity, but the Presbyterian Hospital records contain the description of an old woman dying in an extremely emaciated state whose entire small intestine was the seat of multiple submucous lipomas bright yellow in color and made up of solidly packed masses of normal appearing fat cells. Wells has not been able to detect any chemical difference between normal and neoplastic fat and cannot explain the phenomenon.

There is a bizarre and unexplained fact noted in connection with liposarcoma of the kidney itself. Some ten cases have been recorded (4 by Fischer and 1 each by Froug, Harbitz, Hartwig, Lubarsch, McCartney and Wynne, and Judd and Donald). The six cases of Fischer, Froug and Harbitz occurred in individuals suffering from tuberous sclerosis and adenoma sebaceum (Pringle) of the face. The records of the Squier Urological Clinic of this Medical Center contain another example of this bizarre association in a young woman who is still alive. The classical paper on the subject is by Fischer, who described other types of neoplastic malformations in the kidneys of patients with tuberous sclerosis as well as multiple lipomas and liposarcomas.

In addition to their sometimes enormous size, liposarcomas are notable for their variation in growth rate, which occasionally is very rapid and at other times exceedingly slow. An excellent example of slow growth is recorded by Martin and Colson. Symptoms commenced at 23 years when the woman began to have pains in her thigh. At 36 the thigh began to swell. At 38 a huge tumor was removed which extended from Scarpa's triangle back to the gluteal fold and forced her to keep the extremity in abduction. The mass was excised in two parts from beneath the deep fascia. Grossly, it looked

like salmon paste (laitance) and was called either round cell sarcoma or malignant lipoma. Six years later, at age 44, a recurrent mass was removed from beneath the gluteal fold which was soft, diffluent and the color of wet chamois skin. At this time roentgenograms showed rarefactions of the ischium and femur. The next operation was performed 16 years later, when she was age 60. Pieces of the tumor were removed but she died of shock. At autopsy, the tumor surrounded the hip joint, invaded the adjacent bones and passed into the pelvis through the obturator foramen. There is no mention of metastases. This story represents the probable course of a very considerable number of liposarcomas provided it is not interrupted by death or cure. It is of interest that the tumor secondarily invaded bone, because several cases reputed to have been primary in bone formed bulky extra-osseous tumors around relatively small bony lesions, and one wonders if in these cases the bony involvement may not have been secondary (L. Barnard, Fender, Rehbock and Hauser). Indeed, the whole question of the origin of liposarcomas in bone marrow needs further investigation and confirmation from other sources than the one which has sponsored either directly or indirectly almost all of the cases published. The cases originally published by Stewart were challenged by the late W. G. Barnard, and one must acknowledge that they seem different from liposarcomas arising in other tissues.

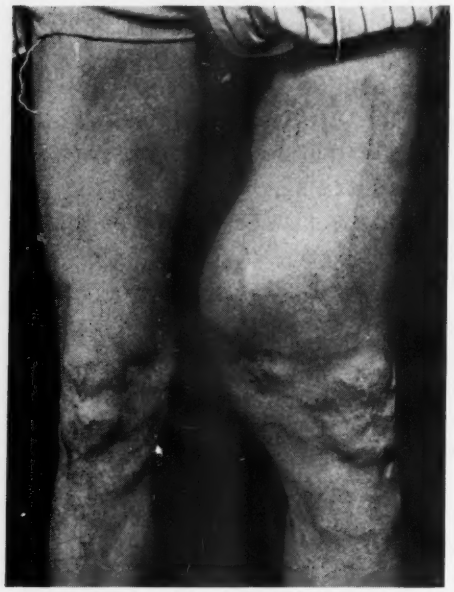

FIG. 2.—Case 7: Undifferentiated myxoid liposarcoma of thigh. A characteristic example of these bulky tumors.

Some liposarcomas pursue a much more rapid course, as exemplified by several cases in the present series, *e.g.*, Case 7 (Figs. 2 and 3), which attained a size of 24 by 16 cm. in the thigh in six months and caused death by extension and metastasis five months after amputation; Case 9, the total known duration of which was only ten months, and Case 16, which reached a size of 14 x 12 cm. in the buttock in six months and resulted in death with intra-abdominal and lung involvement in another six months. Between these extremes there are all grades of variation, but with the greater number exhibiting slower growth and with a relatively small number spreading by metastasis. Before the question of metastasis can be debated, the extremely interesting subject of the multiplicity of tumors must be elaborated for the two inevitably become confused one with the other.

It is well known that lipomas are often multiple; occasionally one or

more of these fatty tumors develop in the body and, succeeding them, many other tumors appear as if they were metastases. Lubarsch's case is representative of one type. There was a large multinodular fibrous and fatty tumor in the left perirenal region with many smaller similar foci in the kidney itself, retroperitoneal region, suprarenal gland, liver, heart, subpleura, left lung, periaortal and retro-esophageal areas, spinal vertebrae and both femora. In spite of the benign appearance he believed these small foci were metastases. Siegmund described a very similar case except that the secondary nodules

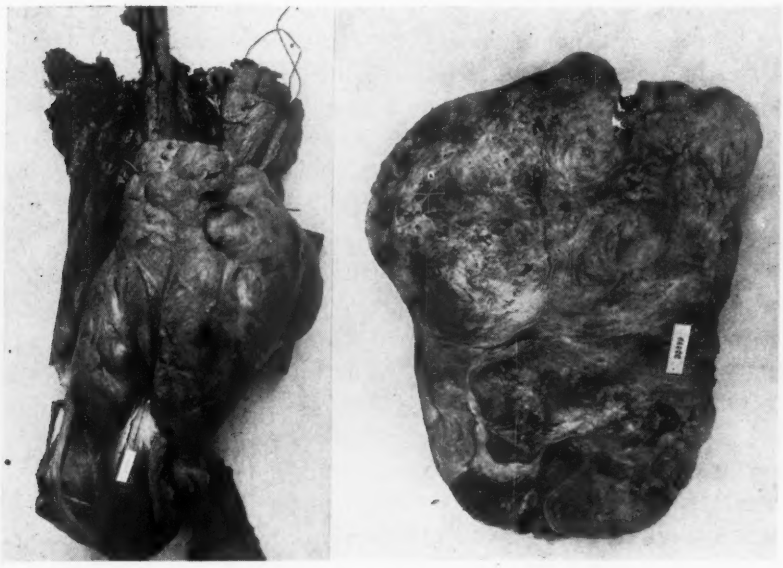

FIG. 3.—Case 7: The tumor lay deep to the sartorius, semimembranosus and vastus medialis muscles which have been dissected away to expose it. At the right the cut surface of the tumor is shown.

appeared like liposarcomas. He believed that both his own and Lubarsch's cases were examples of multiple tumors and not metastasis formation. Somewhat comparable cases have been recorded by Goormaghtigh, *et al.*, who favor the metastasis hypothesis and by Martland, Gold, and Sternberg, all of whom preferred to believe that the tumors were independent. Somewhat more frequent are instances in which a few more or less widely separated liposarcomas appear simultaneously or successively, and one must decide whether they are independent or represent metastases. An excellent example is Case 15 in the present series, previously reported by Murray and Stout. The first tumor appeared in the antecubital fossa and two and one-half years later a second tumor developed higher up in the arm. In Case 32 there were three entirely separate liposarcomas in the thigh, the popliteal space and in the pelvic retroperitoneal space. In Case 7, following amputation for a thigh liposarcoma, the patient died with tumors in the pelvis, back, gluteal region and cerebrum. The cerebral tumor must have been a metastasis but

should one accept the other three nodules as extensions, metastases or separate tumors? Similar problems arise with regard to cases reported by Hosemann and Lang, Josephson and Westberg, and Narr and Wells. It seems to the writer that in the majority of the above quoted cases one is dealing probably with multiple independent tumors. The question is of more than academic importance for it has some bearing on the choice of treatment.

The preceding paragraph indicates that there are some cases in which apparent metastases may only be multiple tumors. It should not be interpreted as meaning that metastases never occur in cases of liposarcoma, for most certainly they do. In addition to one example each by the five reporters of bone liposarcomas, unquestionable metastases are recorded by Daniel and Babès, Geschickter, Gricouroff, Harbitz, Jaffé, Lepoutre, Lifvendahl, Menne and Birge, Moreland and McNamara (2 cases), Nieuhuis, Seids and McGinnis (2 cases), Stich, Taussig, Vincent and Sénellart, Virchow (1857 and 1865), and Waldeyer. To these may be added Cases 3, 6, 7, 9, 14, 16, 26, and 34. From the data at hand, it is impossible to determine the relative frequency of metastases because there exists no series of consecutive cases followed over a long enough period to be of statistical significance. The impression one gains from the literature is that metastases are less common than with other types of sarcoma since among 134 cases there are only 24 with metastases, and if one subtracts the eight bone cases from the total then there are only 19 among 126. If one takes the Presbyterian Hospital cases, most of which have been followed, and excludes the last four which have occurred within the last two years; there remain 17 cases of which six have shown metastases. If Cases 2, 4 and 11 are also subtracted because they represent examples of the well differentiated form of liposarcoma, often called myxolipoma or some comparable name, there are then six metastatic cases among a group of 14, or 40 per cent. This figure is probably somewhere near the truth. In 60 per cent of cases metastases lodge in the lungs or pleurae, in 25 per cent in the liver, after which come bone marrow and central nervous system, with isolated examples of involvement of other scattered parts. In no single acceptable case were there widespread metastases—a further argument against the acceptance of the cases of Lubarsch and Siegmund as ones of extensive metastasis rather than multiple tumors.

The gross characteristics of liposarcomas are quite varied, but in general they form large bulky, nodular, masses of apparently encapsulated tissue which is always firmer than the adipose tissue of simple lipomas and runs a gamut of colors from orange to pale cream often with an admixture of reds caused by areas of increased vascularity or hemorrhage (Fig. 3). Somewhat more than half of them are slimy and mucoid (Fig. 4). These tumors not infrequently have areas of normal yellow fat interspersed among the sarcomatous masses. In a few tumors there are dense fibrous areas. Occasionally degeneration cysts may form but this is exceptional and even the colossal tumors usually remain solid throughout in spite of extensive areas of degeneration. Secondary or local multiple nodules are probably quite frequent and account

for the many times which local recurrences manifest themselves after attempted excision.

The microscopic features of liposarcomas are even more varied than the gross and unfortunately have given rise to a great variety of names which make for confusion and misconception. Ewing (1935) gives us a basic separation of liposarcomas into two main types: One, the myxoliposarcoma, which is vascular, myxoid and lipoblastic; the other, the granular cell lipoblastoma composed of cells resembling the foamy lipoblasts of brown fat. With this recognition of two forms of lipoblasts, all who have had any degree

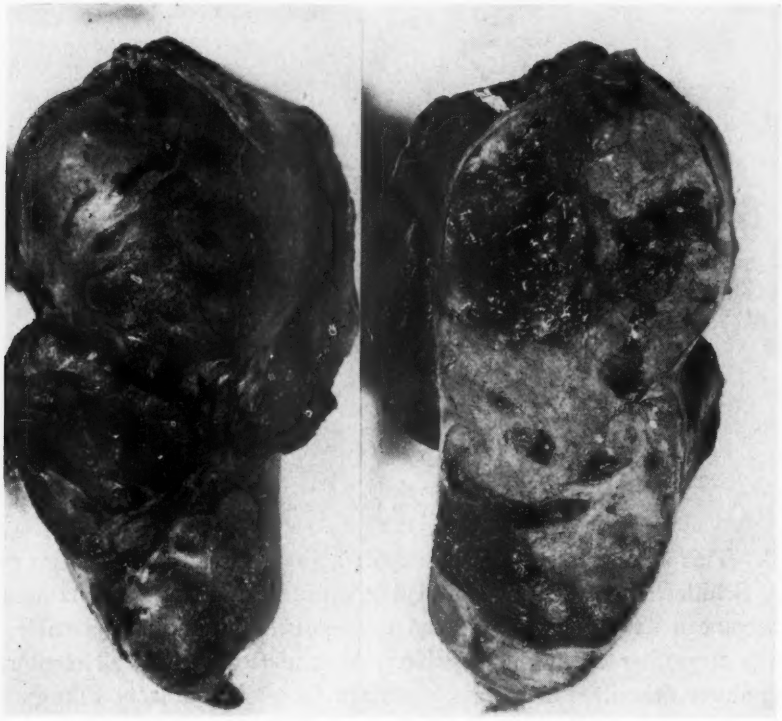

FIG. 4.—Case 12: Undifferentiated myxoid liposarcoma after its removal from within the gastrocnemius muscle. The highlights of the cut surface at the right represent slimy mucoid material.

of experience with these tumors will agree but will demand further elucidation. How, for instance, can one distinguish between what is so frequently called myxolipoma, fibromyxolipoma or some similar name and Ewing's myxoliposarcoma? The answer to this query is that one cannot, because, as Gricouroff has pointed out, the *"lipome embryonnaire"* or myxoid lipoma can behave like a malignant tumor by recurring and metastasizing. He places them between simple lipomas and atypical liposarcomas. Mucicarmine will stain the intercellular substance but never intracellular vacuoles which contain lipoid. He points out that these tumors may have areas resembling fibrosarcomas poor in collagen as well as myxoid areas. Jaffé also recognizes

these three different variants which he called respectively lipoblastomas, lipoma pseudomyxomatodes and liposarcoma but he was apparently not aware that the first tumor form might recur after excision and the second both recur and metastasize. Moulonguet and Pollosson also have three divisions of lipoblastic sarcoma which they call respectively malignant lipoma, lipoblastic myxoid sarcoma and lipo- and fibroblastic sarcoma.

This attempt to divide the malignant fat-forming tumors into three separate and distinct groups is doomed to failure, however, because when one has a relatively large group to study, such as the 41 cases in the present collection, one finds that all of the cases are not pure types but that some of them are

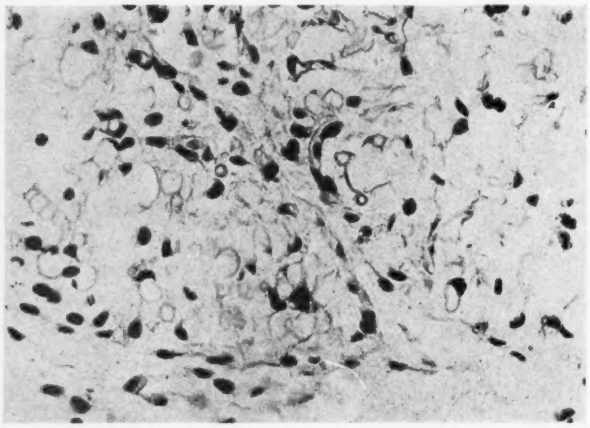

FIG. 5.—Embryonal fat from the subcutaneous layer of a supernumerary finger removed a few days after birth.

mixed. This should have been anticipated, since it has already been pointed out by Schiller, and others, that a benign lipoma can change its characteristics and become a malignant tumor, and if one such mutation is possible, theoretically any other change is possible. As a matter of fact, all combinations of the above described histologic types are found in different tumors of this series. For example, both myxoid and round cell (adenoid) areas are found in different parts of Cases 5, 8, 17, 22, 24, 28, and 29; combinations of myxoid and fibrosarcomatous areas in Case 25; myxoid, round cell and fibrosarcoma-like areas in Case 14; and areas of osseous and cartilaginous metaplasia in an otherwise myxoid tumor in Case 40. The fact that both myxoid and adenoid or round cell developments may be found in the same tumor seems to be an observation of some importance. It indicates that there are probably not two separate and distinct ancestral lipoblasts, one of which forms ordinary adipose tissue and the other brown fat, but that the same ancestral cell in the primitive mesenchyme is capable of forming either or both—certainly, Figures 11 and 12 show that the two types can be so juxtaposed in the same tumor that one can hardly credit that they were formed by two different cell prototypes. If this is true it should lead

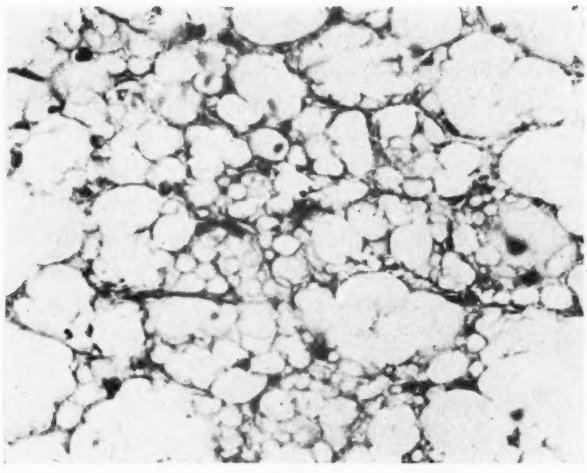

FIG. 6.—Brown fat from the deep fatty tissues of the lateral neck region of a male, age 41.

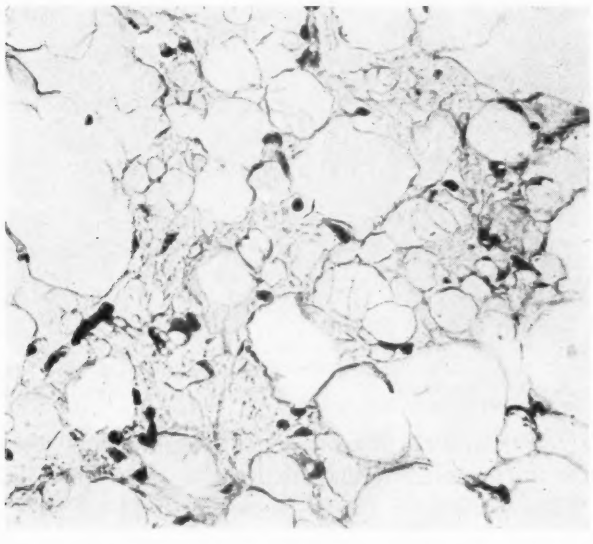

FIG. 7.—Case 19: Differentiated myxoid liposarcoma. The photomicrograph shows embryonal lipoblastic tissue, resembling the embryonal fat shown in Figure 5, mixed with adult fat cells.

us to look upon the liposarcomas not as a group of separate and distinct tumor types worthy of bearing separate names but as a single group capable of manifesting different degrees of differentiation which can be indicated by descriptive adjectives. Since this group represents the malignant form of the fat-forming tumor it is quite properly called liposarcoma. With this conception in mind, liposarcomas may be subdivided as follows:

1. *Well Differentiated Myxoid Type:* This resembles the usual type of embryonal fat (Figs. 5 and 7). It consists of adult fat cells, embryonal stellate- or spindle-shaped fat cells containing droplets of a material which can be

stained with scharlach R. or sudan III, and usually a rather rich network of capillaries. The whole mass is bound together by a loose meshwork of connective tissue which is generally, but not always, slimy and myxoid. Sometimes this slimy material can be tinted with mucicarmine and sometimes not. This characteristic picture is occasionally varied by the presence of more or less dense fibroblastic tissue with well developed collagen and reticulin fibers. The lipoblasts whether stellate- or spindle-shaped are rather small, regularly formed and, although such tumors may be enormous, it is almost impossible to detect any mitoses. It is questionable whether such tumors ever metastasize while they remain in this state of good differentiation. Cases 2, 4, 11, 19, 31, 36, 37 and 41 are examples.

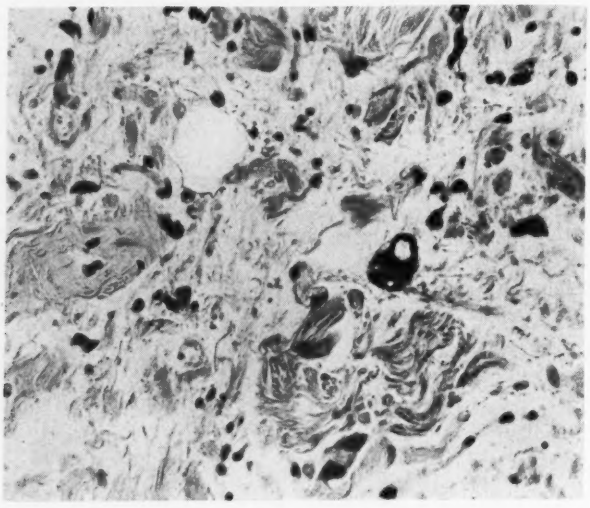

FIG. 8.—Case 10: Undifferentiated myxoid liposarcoma. The lipoblasts are bizarre with hyperchromatic nuclei. The stroma of this tumor is quite fibrous.

2. *Poorly Differentiated Myxoid Type:* This group resembles the first group, with the important difference that the lipoblasts are bizarre and often monstrous. They grow to a large size with astonishingly variable nuclear formations and the misshapen nuclei are often hyperchromatic or pyknotic (Figs. 8 and 9). As noted by Murray and Stout, such cells are usually degeneration forms and incapable of reproduction *in vitro*. The bizarre lipoblasts often dominate the picture and the amount of lipoid produced is correspondingly less. Signet-ring forms are occasionally seen. Completely differentiated adipose tissue is less or entirely absent and the number and arrangement of blood vessels so variable as to be no longer significant. Fibrosarcomatous areas are sometimes produced (Fig. 14). This poorly differentiated type is definitely malignant, difficult to eradicate, and may metastasize. It is represented in this series by Cases 1, 6, 7, 9, 10, 12, 13, 15, 18, 19, 20, 21, 23, 26, 30, 32, 33, 34, 35, and 40.

3. *Round Cell or Adenoid Type:* The characteristic lipoblast of this tumor type is rounded with centrally placed nucleus and voluminous foamy cytoplasm,

the vacuoles of which are filled with lipoid. The cells are massed together in close approximation with only a delicate fibrous framework and an inconspicuous blood supply (Figs. 10, 11, and 12). In many such tumors the cells may reach an enormous size. Jaffé measured them as large as 120 microns and the cell illustrated in Figure 13 is 126 microns in length. The hyperchromatic pyknotic nuclear material indented by the vacuoles suggests that these are degeneration forms. These tumors are not myxoid. Like the tumors of the second group they are difficult to eradicate and may metastasize. Cases 3, 16, 27, 38 and 39 are examples of this group.

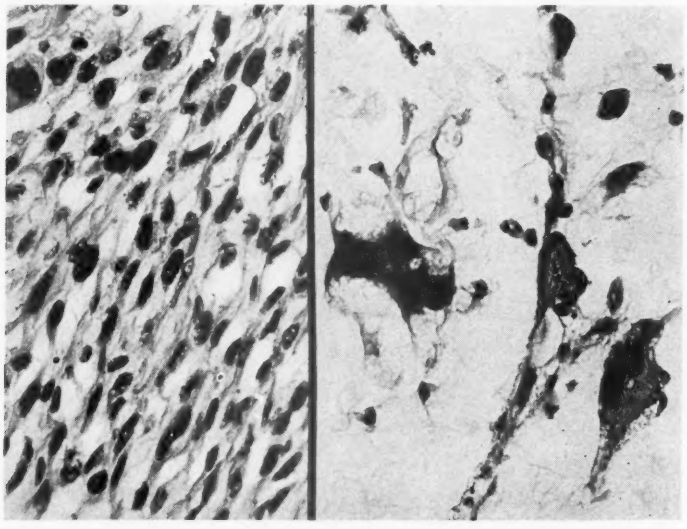

FIG. 9.—Case 35: Undifferentiated myoid liposarcoma. At the right are bizarre lipoblasts partly filled with vacuoles in a mucoid stroma. At the left, the lipoblasts are elongated, probably because there is little intercellular material and they tend to be compressed.

4. *Mixed Group:* These are the tumors composed of two or more elements of the preceding groups. They, too, are definitely malignant (Figs. 10, 11, 12, 14). Representatives are Cases 5, 8, 14, 17, 22, 24, 28 and 29.

Diagnosis of any tumor should be made with accuracy before it is treated. Liposarcomas can be suspected clinically if they have reached a very large size and with some degree of certainty at exploration if in addition the tumor is both yellow and slimy. But the only proper procedure is biopsy before treatment, confirmed by immediate frozen section if possible, if not by paraffin section. Progress in the treatment of soft part tumors will never be attained if this is not made a routine procedure instead of the all too common method of excising the whole tumor first and secondarily trying to carry out some further and more radical procedure if the growth proves to be malignant. Liposarcomas have such distinctive histology that the only tumor with which they may easily be confused is the myxoma. The myxoma has no lipoblasts and no fat is formed. The differentiation between the two is worth while because the myxoma, while it may continue to grow if not completely excised, never metastasizes, so far as this writer is aware.

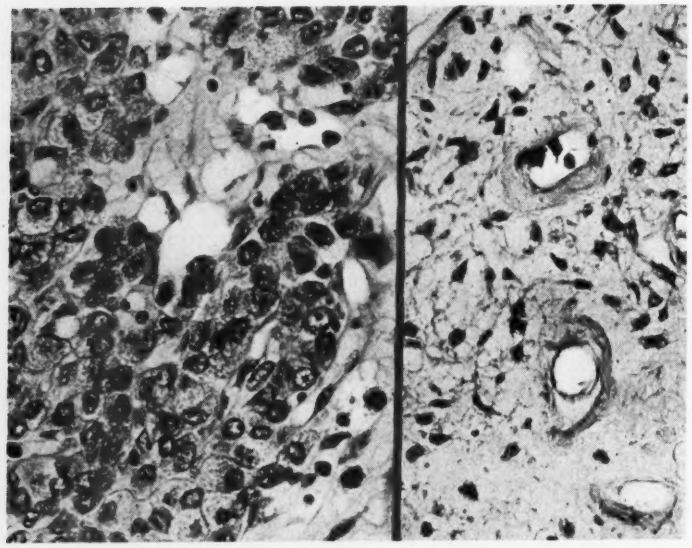

FIG. 10.—Case 24: Mixed myxoid and round cell liposarcoma. At the right a myxoid area is shown resembling the embryonal fat shown in Figure 5. At the left is the junction between a myxoid and round cell area. The rounded lipoblasts are honeycombed with tiny lipoid vacuoles.

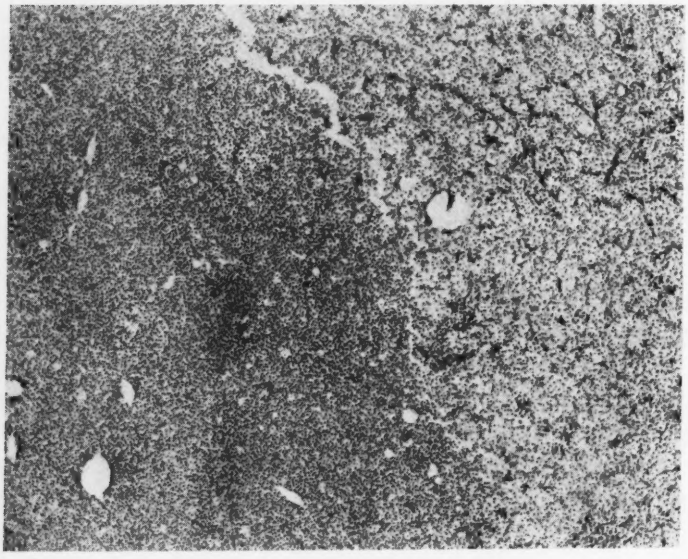

FIG. 11.—Case 8: Mixed myxoid and round cell liposarcoma. At the left is shown the solid mass of rounded lipoblasts. At the right is the loose-textured vascular myxoid portion of the tumor.

Treatment of liposarcomas is primarily surgical but it should be pointed out that some liposarcomas have proved to be definitely radiosensitive, and for this reason radiotherapy as a mode of treatment must not be neglected. Ewing (1935) has recommended that it be used before any operation. In Cases 12 and 15 of this series it was used on relatively small recurrent nodules with success lasting seven years and five months in the former and two and one-half years in the latter. Radiotherapy was used in six other Presbyterian Hospital cases either without any benefit or with only temporary effect. It should be noted that the good results were obtained with rather small recurrent masses in easily accessible situations while the failures were

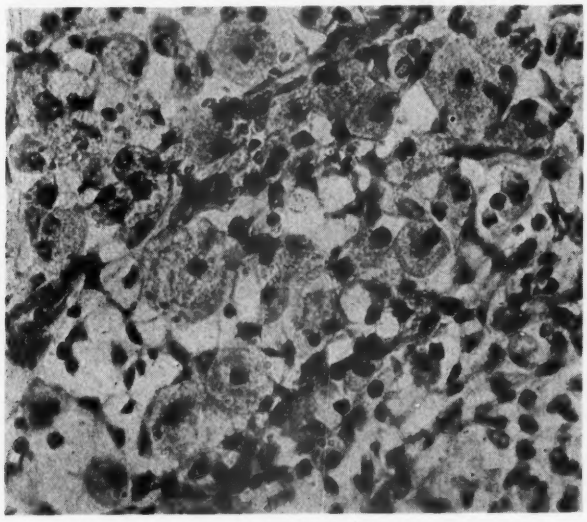

FIG. 12.—Case 8: Details from the junction of the two cell types shown in Figure 11. The rounded, finely vacuolated lipoblasts are intermingled with the stellate and elongated cells of the myxoid area.

in larger and usually deeper tumors. The details are recorded elsewhere in this paper. Reports from other clinics are discouraging. It was used postoperatively to prevent or because of recurrences by Moreland and McNamara in two cases, by De Renzi, Selman, and Seids and McGinnis in one case each, with complete failure. Another case treated by Seids and McGinnis postoperatively was without recurrence at the end of one year; too short a time to be significant. Siegmund treated some of the many tumors in his case with roentgenotherapy and reported partial and temporary regression. In spite of this, one should be encouraged to believe that since some success has been obtained at the Memorial Hospital and in this institution, this is a form of treatment which should not be abandoned.

If a tumor is a well differentiated myxoid liposarcoma, one does not need to be as radical as for the other three groups, because the worst that may be expected is local recurrence. Nevertheless, it will pay to treat even these tumors with respect and remove the entire capsule and the tissue

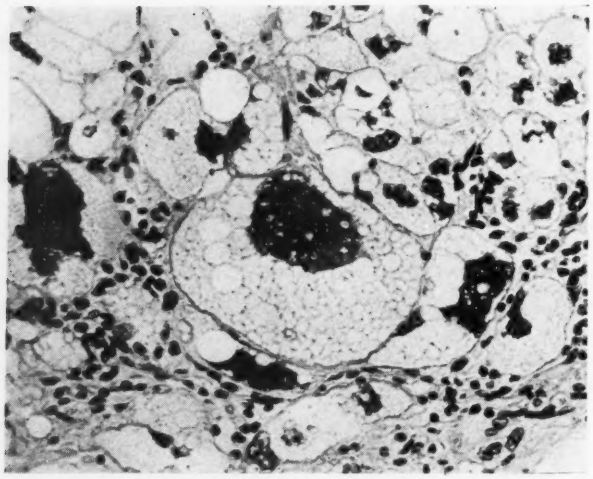

FIG. 13.—Case 27: Detail of a round cell liposarcoma showing giant lipoblasts. The large cell in the center is 126 microns in length. It is probable that these huge cells are degenerate and incapable of reproduction.

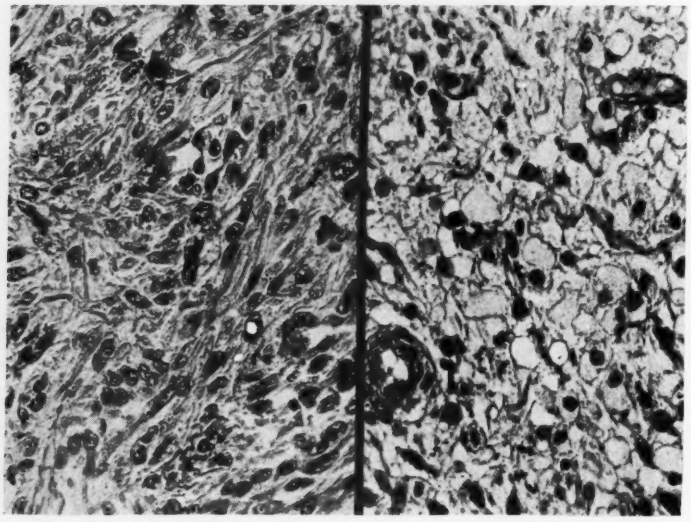

FIG. 14.—Case 14: Mixed myxoid and round cell liposarcoma. At the right a myxoid area with intermingled round cell lipoblasts. At the left an area where the cells simulated the appearance and arrangement of a fibrosarcoma.

immediately outside of it because one can never be absolutely sure that the entire tumor is well differentiated, or that a recurrence may not be less well differentiated and more malignant. The ease with which a second nodule may be overlooked is illustrated by Case 19. An apparently encapsulated tumor attached to the deep fascia was enucleated from the thigh with the diagnosis of lipoma. When the microscope showed that it was a liposarcoma, the whole area was reexcised. In the gross specimen, a second deeper entirely unsuspected nodule of similar type was discovered.

TABLE I

RECORD OF CASES*
PRESBYTERIAN AND ALLIED HOSPITAL CASES

Case No.	Sex	Age	Site	Duration Before Diag. Mos.	Size—Cm.	Type	Treatment	Result
1	F	65	Lumbar	?	?	Myxoid (undiff.)	Excision	?
2	F	43	Canal of Nuck	5	12 x 7 x 2	Myxoid (diff.)	Excision	No recur. 22¼ years
3	M	33	Retroperitoneal (psoas-iliacus musc.)	3	21 x 17 +	Round cell	Partial excision. Radiotherapy	Died 15+ months. Lung and liver metastases
4	M	38	Back of neck	12	7 x 6	Myxoid (diff.)	Excision	No recur. 17½ years
5	F	29	Back	120	4 x 2.7	Myxoid (undiff.) and round cell	Excision	No recur. Died 45 mos. myocarditis
6	F	60	Omentum	0.75	"very large"	Myxoid (undiff.)	Biopsy	Died postop. Metas. in liver and pleurae
7	M	59	Thigh	6	21 x 16	Myxoid (undiff.)	Biopsy. Amputation	Died 5 mos. Metas. to cerebrum. Tumors in pelvis, back & gluteal regions
8	F	55	Thigh	180	21 x 15 x 9	Myxoid (undiff.) and round cell	Excision. Radiotherapy	Recurred. Died 42 mos. postop.
9	M	40	Scapular reg.	3	15 x 13	Myxoid (undiff.)	Excision. Biopsy recur. Radiotherapy	Died hemorrhage 7 mos. postop. Metas. to lungs & extension to axilla
10	M	66	Cheek	24	3 x 2 x 1	Myxoid (undiff.)	Excision	No recur. 15 mos. postop. died "heart disease"
11	M (colored)	37	Temporal reg.	96	8 x 8 x 4	Myxoid (diff.)	Excision	6 years, 3 mos.—no recurrence
12	F	59	Leg (gastrocn. mus.)	7	12.5 x 6	Myxoid (undiff.)	Excision. Radiotherapy of reputed recur.	Reputed local recur. at 15 mos. 8 yrs., 8 mos. after op. no definite disease
13	F	57	Retroperitoneal	132	42 x 22 x 18 (wt. 28 lbs.)	Myxoid (undiff.)	Biopsy	Died postop. No metastases
14	M	32	Thigh	4	15 x 11	Myxoid (undiff.) with areas like fibrosarcoma and round cell	Excision. Reexcision. Radiotherapy	Died 67 mos. after 1st op. with recur. and lung metastases
15	M (colored)	64	Forearm	5	20 x 8 x 6	Myxoid (undiff.)	Excision. Excision of 2nd tumor. Radiotherapy of recur.	2nd tumor in arm and recur. in forearm after 30 mos. No evidence of tumor 60 mos. after 1st op.
16	M	74	Gluteal	6	14 x 12	Round cell	Biopsy. Radiotherapy	Died 6 mos.—lung met. and intra-abdominal tumor.
17	F	52	Thigh	3.5	16 x 16	Myxoid (undiff.) and round cell	Biopsy	Died 1 mo.—hemorrhage.
18	F	75	Perirenal	12+	15 x 15	Myxoid (undiff.)	Excision. Nephrectomy	Died 3 mos.
19	F	46	Thigh	3	4 x 3 & 2.7 x 1.5	Myxoid (diff.)	Excision in 2 stages	Recovered
20	M	49	Thigh (intramuscular)	24	27 x 18 x 11 (wt. 7.5 lbs.)	Myxoid (undiff.)	Biopsy. Excision	Recovered
21	M	86	Retroperitoneal (above bladder)	7	8 x 8	Myxoid (undiff.) (within larger lipoma)	Excision	Recovered

TABLE I—(*Continued*)

CASES FROM OTHER SOURCES

Case No.	Sex	Age	Site	Duration Before Diag. Mos.	Size—Cm	Type	Treatment	Result
22	F	Adult	Arm	?	4 x 3 x 2	Myxoid (undiff.) and round cell	Excision	?
23	F	28	Thigh	?	Unknown	Myxoid (undiff.)	Excision	Local recur. after 4 yrs.
24	M	50±	Popliteal space	6	16 x 15	Myxoid (undiff.) and round cell	Excision	No recur. after 4 years
25	M	?	Forearm	?	Unknown	Myxoid (undiff.) with areas like fibrosarcoma	Excision	?
26	M	60	Popliteal space	24	18 x 12 x 8	Myxoid (undiff.)	Excision. Radiotherapy	Died with met. after 3 yrs., 2 mos.
27	M	62	Inguinal	2	10 x 10±	Round cell	Partial excis.	?
28	F	62	Back	3	20 x 13 x 5	Myxoid (undiff.) and round cell	Excision	?
29	M	55	Popliteal space	2	12.5 x 10 x 10	Myxoid (undiff.) and round cell	Excision	?
30	?	?	Leg	?	?	Myxoid (undiff.)	Excision	?
31	M	67	Scrotum, canal & pelvic retroperitoneum	48±	Large	Myxoid (diff.)	Excision	?
32	M	54	(1) Thigh (2) Pop. space (3) Pelvic retroperitoneum	144	(Retroperit. Weighed 1–2 kilos)	Myxoid (undiff.)	Excision of all 3	?
33	?	?	Leg	?	8.5 x 8	Myxoid (undiff.)	Amputation	?
34	F	58	Popliteal space	12	16 x 9	Myxoid (undiff.)	Biopsy. Excision	Died with metastases
35	M	50	Axilla	0.5	12 x 12	Myxoid (undiff.)	Excision	?
36	M	Adult	Cheek	?	3.2 x 2 x 1.8	Myxoid (diff.)	Excision	?
37	M	50±	Lumbar	?	?	Myxoid (diff.)	Excision	?
38	F	18	Gluteal	6±	8 x 7 x 6	Round cell	Excision. Radiotherapy	9 years no recurrence
39	M	57	Infraclavicular (also ca. mammary gland)	?	?	Round cell	Excised	?
40	M	68	Gluteal (intramuscular)	2	19 x 13 x 5.5	Myxoid (undiff.) (with bone & cartilage metaplasia)	Excised	?
41	F	50	Orbit	1	?	Myxoid (diff.)	Excised	?

*These cases have the following origins: Case 22 from Vanderbilt Clinic, New York, Dr. P. R. Turnure; Case 23 from Roosevelt Hospital, New York, Dr. W. C. White; Cases 24 and 25 from Lincoln Hospital, New York, Dr. Chester R. Brown; Cases 26, 28, 30, 31, 35, 36 from the Nix Hospital Laboratory, San Antonio, Texas, Dr. A. O. Severance; Case 27 from the New York Postgraduate Hospital, Dr. M. N. Richter; Case 29 from the Hospital for Ruptured and Crippled, New York, Dr. H. Pheasant; Case 32 from Ellis Fischel State Cancer Hospital, Columbia, Mo., Dr. L. V. Ackerman; Case 34 from Cornwall Bridge, Connecticut, Dr. W. C. Clarke; Cases 37 and 41 from the Hospital of the University of Pennsylvania, Dr. R. C. Horn; Case 38 from the Mather Hospital, Port Jefferson, L. I., Dr. Ethel Trygstad; Case 39 from Bellevue Hospital, New York, Dr. W. G. von Glahm; Case 40 from Vassar Bros. Hospital, Poughkeepsie, N. Y., Dr. Elizabeth Heath.

DETAILS OF CASES TREATED WITH RADIOTHERAPY

Case 3.—One month after operation six radiotherapy treatments were given in the course of two weeks. Factors unknown. No effect.

Case 8.—Immediately after operation eight treatments were given during a period of three and one-half months through anterior and posterior 15 x 20 cm. fields to thigh and hip, totalling 2300 r. with the following factors: 200 kv, 50 cm. skin distance, 8 ma., 1.86 mm. cu. + 1 mm. al. Sixteen months later after the tumor had reappeared, 16 more treatments were given to 20 x 25 cm. anterior and posterior thigh and hip fields, totalling 4800 r. The factors were: 195 kv, 50 cm. skin distance, 8 ma., 1.86 mm. cu. + 1 mm. al. Eight years before operation the original tumor had been treated elsewhere with roentgenotherapy without effect. The treatment of the recurrence had no effect.

Case 9.—The treatment given was to a large rapidly growing local recurrence and axillary extension. 2790 r. was first given to the recurrent mass. Factors: 200 kv, 30 ma., 50 cm. skin distance, filter ½ mm. silver and 1 mm. of aluminum. This caused some shrinkage. Three months later, using the same factors, 1860 r. were given through anterior and posterior fields to the axilla. This was supplemented after 3 months with 4900 mg. hrs. of radium in 3.5 cm. radium needles. The effect was slight and probably did not retard the fatal termination.

Case 12.—When a 2.5 x 2 cm. mass appeared in the scar 15 months after excision this was assumed to be a recurrence. This was treated through two 8 x 10 cm. fields, a total of 6000 r. in 40 days was given. Factors 200 kv, 25 ma., skin distance 50 cm. filter 2 mm. cu. + 1.25 mm. al. This caused complete disappearance of the mass and it has not reappeared in the succeeding 7 years and 5 months.

Case 14.—Roengenotherapy was begun after a recurrent tumor mass was excised with resection of the sciatic nerve from the posterior thigh. During a period of 5 months through two 10 x 15 cm. and one 8 x 12 cm. fields a total of 9000 r. was given. Factors 190 kv, 8 ma., 50 cm. skin distance; 1.31 mm. cu. + 1 mm. al. filter. One year after the termination of the first course there was no local tumor in the thigh but a mass could be felt deep in the iliac fossa. A second course was begun using three 15 x 15 cm. fields in the thigh and hip regions. It was continued for 3 months, and a total of 9000 r. was given with the following factors: 200 kv, 25 ma., 50 cm. skin distance, filter 1.05 mm. cu. + 1.25 mm. al. This did not prevent the tumor from persisting and slowly filling the pelvis. Two months after the termination of the second course a little more irradiation was given to the abdomen and pelvis, totalling 975 r. All of this failed to check the progress of the disease to a fatal termination.

Case 15.—Details of radiotherapy given in paper by Murray and Stout.

Case 16.—The roentgenotherapy given in this case represents treatment of the tumor begun 3 days after biopsy. Three 10 x 15 cm. fields were used and a total of 7000 r. given in a period of 40 days. The factors were: 200 kv., 25 ma., skin distance 50 cm., filter 1 mm. cu. + 1 mm. al. The patient left the city before any more treatment could be given. It did not check the progressive growth of the tumor and the rapid fatal termination.

Case 20.—This represents postoperative prophylactic radiotherapy. Two 8 x 20 cm. and two 10 x 20 cm. fields were used and a total of 8000 r. given in a period of 54 days. The factors were: 200 kv, 25 ma., 50 cm. skin distance, filter 1 mm. al. + 1 mm. cu. The case is too recent to have any significance.

The principle of treatment for all other liposarcomas should be radical surgery, if a cure is to be attempted. Failures are bound to occur, however, in some cases, such as the retroperitoneal tumors, because their situation makes complete removal impossible, and in others because there may be undiscovered multiple tumors. In many cases this may not result in immediate death even with recurrence, because so many of these tumors progress slowly and fail to metastasize. It would seem not worth while to attempt very extensive and shocking operations in the very old and infirm because the risk of operative death may be greater than the untoward results which may follow more conservative treatment of the tumor. One cannot establish rules to govern the treatment of every individual case, because the factors are so many and so varied. One can only keep in mind the possibilities when treatment is planned.

SUMMARY

A group of 41 cases of liposarcoma has been studied in connection with 134 previously reported cases. These tumors tend to form very large bulky masses, with a predilection for the thigh and extraperitoneal tissues but with occasional appearance in many other regions as well. They exhibit great variations in growth speed, they are sometimes multiple and the more malignant forms metastasize usually either to the lungs or liver.

Grossly, these tumors are frequently mottled with yellow because of their lipoid content and are often slimy from the formation of mucoid material. Microscopically, they can be divided into one well differentiated, less malignant group, which simulates the appearance of ordinary embryonal fat and three other poorly differentiated more malignant groups resembling respectively atypical ordinary embryonal fat, atypical brown fat with the formation of rounded lipoblasts, and finally a group showing both of these elements in combination. Probably as a result of metaplasia these tumors can on occasion form other tissues such as reticulin and bone. This versatility suggests that there are probably not separate embryonal stem cells for adipose tissue and brown fat but that both spring from a common ancestor segregated from the primitive mesenchyme.

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TABLE VI

Case No.	Sex	Age	Site	History	Duration	Physical Findings	Laboratory Findings: Blood	Gastric	Sto
1	F	62	Esophagus	Vomiting; epigastric pain; 60 lb. wt. loss	5 mos.	Emaciation			
2	F	54	Stomach	Weakness; pallor; tarry stools; vomiting	2 wks.		Hb. 11 Gm. R.B.C. 3.5	Low acid	
3	F	51	Stomach	"Indigestion"	3 mos.	Epigastric tenderness		Normal	Guaia positi
4	F	43	Stomach	Epigastric pain; nausea, vomiting; 40 lbs. wt. loss	9 mos.	Nontender epigastric mass	Hb. 9.5 Gm. R.B.C. 3.8	Ana-cidity	
5	M	58	Stomach	Epigastric pain; 10 lb. wt. loss	3 mos.	Tender epigastric mass		Low acid	Guaia positi
6	F	65	Stomach	Epigastric pain; mass; nausea; tarry stool; 9 lb. wt. loss	4 mos.	Cervical node. Tender epigastric mass; mass in cul-de-sac T. 38.6° C.	Hb. 9.5 Gm. R.B.C. 3.3	Low acid	Guaia positi
7	M	52	Stomach	Nausea, vomiting; epigastric pain; tarry stools	2 wks.	Negative	W.B.C. 13,600	Normal	Guaia positi
8	M	58	Stomach	Anorexia; upper abd. pain; 20 lb. wt. loss	3 mos.	T. 38.° C.; axillary mass; tender epigastric mass	Hb. 12 Gm. R.B.C. 3.8		Guaia positi
9	M	33	Jejunum	Epigastric pain, vomiting, tarry stools, 30 lb. wt. loss	3 mos.	General lymphadenopathy. T. 39.° C.		Normal	Benzi positi
10	M	5	Ileum	Lower abd. pain; vomiting, bloody stools	1 mo.	General lymphadenopathy	Hb. 8 Gm. R.B.C. 3.1		Benzi positi
11	M	71	Ileum	Intestinal obstruction					
12	M	4½	Cecal region	Abd. pain; vomiting; 9 lb. wt. loss	1 mo.	Mass in L.L.Q.			Guaia positi
13	M	31	Cecal region	Abd. mass; bloody stools; marked wt. loss	1 mo.	Tender R.L.Q. mass; inguinal nodes; emaciation	Hb. 9.6 Gm. R.B.C. 3.4		Guaia positi
14	F	47	Appendix	R.L.Q. pain; nausea and vomiting	2 days	T. 39.8° C.; R.L.Q. tenderness			
15	F	39	Appendix	No. G. I. symptoms					
16	M	37	Transverse colon	L.U.Q. pain; partial obstruction; 18 lb. wt. loss	7 mos.	Inguinal nodes; epigastric mass; L.U.Q. tenderness			Benzi positi
17	M	65	Sigmoid	Abd. pain; bloody stools; 25 lb. wt. loss	1 yr.	Rectal mass; L.U.Q. tenderness; distention	W.B.C. 21,700 Lymphocyt. 58%; Hb. 10.2 Gm.		
18	M	24	Rectum	Rectal bleeding	4 yrs.	Rectal polypus			
19	M	20	Rectum	Pruritus ani	1 yr.	4 rectal polypi; inguinal nodes			
20	M	45	Rectum	"Constipation"	1 yr.	Rectal mass			

*Died of hypertensive cardiovascular disease with no evidence of recurrence.

**Had left radical mastectomy for adenocarcinoma of breast with axillary metastases 2 yrs. after resection of esophagus; discharge

0 at end of column denotes solitary tumors.

x at end of column denotes regional node involvement without widespread metastases.

xx at end of column denotes metastases upon first examination, some with regional nodes, some without verified regional node involv

TABLE VI

Physical Findings	Laboratory Findings: Blood	Gastric	Stool	Preoperative Diagnosis	
ciation				Carcinoma	Rese esoph
	Hb. 11 Gm. R.B.C. 3.5	Low acid		Carcinoma	Wedg stom
astric tenderness		Normal	Guaiac-positive	Carcinoma	Gastr
tender epigastric mass	Hb. 9.5 Gm. R.B.C. 3.8	Ana-cidity		Carcinoma	Gastr
er epigastric mass		Low acid	Guaiac-positive	Carcinoma	Gastr
ical node. Tender epi-ric mass; mass in cul-de-T. 38.6° C.	Hb. 9.5 Gm. R.B.C. 3.3	Low acid	Guaiac-positive	Carcinoma	Gastr
tive	W.B.C. 13,600	Normal	Guaiac-positive	Carcinoma	Gastr
8.° C.; axillary mass; r epigastric mass	Hb. 12 Gm. R.B.C. 3.8		Guaiac-positive	Lymphosarcoma	Biops
ral lymphadenopathy.),° C.		Normal	Benzidine-positive	Lymphosarcoma	Resec jejun
ral lymphadenopathy	Hb. 8 Gm. R.B.C. 3.1		Benzidine-positive	Intussusception	Ileo-il
				Carcinoma	Ileoco
in L.L.Q.			Guaiac-positive	Intussusception	Reduc suscep
er R.L.Q. mass; in-l nodes; emaciation	Hb. 9.6 Gm. R.B.C. 3.4		Guaiac-positive	Lymphosarcoma	Appen and bi
9.8° C.; R.L.Q. tender-				Appendicitis	Appen
				Lt. ovarian tumor	Appen
inal nodes; epigastric ; L.U.Q. tenderness			Benzidine-positive	Carcinoma	Cecost celioto
l mass; L.U.Q. tender-distention	W.B.C. 21,700 Lymphocyt. 58%; Hb. 10.2 Gm.			Carcinoma	Explor celioto
l polypus				Rectal polypus	Excisi polypu
ctal polypi; inguinal				Fissure in ano	Excisi polypi
l mass				Rectal polypus	Procto biopsy

rence.
y metastases 2 yrs. after resection of esophagus; discharged well.

ad metastases.
h regional nodes, some without verified regional node involvement.

reoperative Diagnosis	Treatment: Operation	Treatment: X-Ray	Pathologic Diagnosis	Follow-up	
cinoma	Resection lower esophagus	No	Small cell lymphosarcoma	Alive and well 2 yrs., 4 mos.**	0
cinoma	Wedge resection stomach	No	Small cell lymphosarcoma	Died.* 7 yrs., 2 mos.	0
cinoma	Gastric resection	Yes	Reticulum cell sarcoma	Alive 3 yrs., 5 mos.	x
cinoma	Gastric resection	Yes	Large cell lymphosarcoma	Died. 1 yr., 10 mos.	xx
cinoma	Gastric resection	Yes	Small cell lymphosarcoma	Alive and well 1 yr.	x
cinoma	Gastric resection	Yes	Small cell lymphosarcoma	Died. 10 mos.	xx
cinoma	Gastric resection	Yes	Large cell lymphosarcoma	Died. 1 mo.	xx
phosarcoma	Biopsy lymph node	No	Large cell lymphosarcoma	Died. 2 wks.	xx
phosarcoma	Resection of jejunum	Yes	Large cell lymphosarcoma	Alive and well 9 yrs., 6 mos.	x
ssusception	Ileo-ileostomy	Yes	Small cell lymphosarcoma	Alive and well. 9 yrs., 5 mos.	x
inoma	Ileocolostomy	Yes	Small cell lymphosarcoma	Died. 6 yrs.	x
ssusception	Reduction of intussusception	Yes	Small cell lymphosarcoma	Died. 4 mos.	xx
phosarcoma	Appendicectomy and biopsy	Yes	Large cell lymphosarcoma	Not followed.	xx
ndicitis	Appendicectomy	No	Small cell lymphosarcoma	4 yrs., 3 mos. Alive and well.	0
varian r	Appendicectomy	No	Giant follicle	Alive and well. 2 yrs., 2 mos.	0
inoma	Cecostomy exp. celiotomy	Yes	Giant follicle	Died. 2 mos., 2 wks.	xx
inoma	Exploratory celiotomy	Yes	Giant follicle	Alive. 4 yrs., 3 mos.	xx
l polypus	Excision of polypus	No	Small cell lymphosarcoma	Alive and well. 2 yrs., 4 mos.	0
re in ano	Excision of polypi	No	Small cell lymphosarcoma	Alive and well. 2 yrs., 2 mos.	0
l polypus	Proctoscopy and biopsy	Yes	Small cell lymphosarcoma	Alive and well. 1 yr., 8 mos.	0

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LYMPHOSARCOMA OF THE GASTRO-INTESTINAL TRACT

REPORT OF TWENTY CASES

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TWENTY CASES of lymphosarcoma of the gastro-intestinal tract have been treated in the New York Hospital during the past nine years. It is with the purpose of bringing out certain points in the treatment and presenting a follow-up study of these cases that this report is made.

No attempt at complete review of the literature will be made. For more extensive reviews, reference may be made to articles by Ullman and Abeshouse, Sugarbaker and Craven, Stout, and Madding and Walker. Stout collected 19 cases of lymphosarcoma of the gastro-intestinal tract encountered over a period of 21 years (1915–1935) at the Presbyterian Hospital in New York. He did not designate the site of occurrence of these tumors but stated that there were six five-year survivals. Madding and Walker reported 41 cases of lymphosarcoma of the stomach from the Mayo Clinic and concluded that the treatment should be surgical removal when possible, with roentgenotherapy administered as an adjunct. Abeshouse and Ullman, in 1932, compiled from the literature reports of 126 cases of lymphosarcoma of the intestines and stated that of 109 in which the site of the lesion was recorded, 77 were in the small intestine (36 in the ileum) and 32 in the large intestine. They found that lymphosarcoma was accompanied by metastases in practically every case. The average duration of life was 19 months for 85 cases upon whom operation was undertaken; ten cases were alive and well five or more years after operation with no sign of recurrence. McCann, in 1930, reported 32 cases of lymphosarcoma of the stomach.

Raiford (1932) reported 88 cases of tumors of the small intestine of which 21 were lymphoblastoma; one was from the duodenum, 18 the ileum and two from sites not determined. Warren and Lulenski (1942) reported 15 cases of lymphosarcoma, 13 of which were subjected to surgery with two apparent five-year cures. The average survival time was 2.5 years.

The relative frequency of lymphosarcoma in the esophagus, duodenum and appendix is attested by reviews such as those of Corner and Fairbanks, Friend, Crowthers, Goldstein, Libman and Eisenbrey. Corner and Fairbanks, in 1904, collected from the literature 14 sarcomas of the esophagus, one a lymphosarcoma which is not described other than by diagnosis. They also cite two instances of "sarcoma" of the appendix without further elucidation. Friend reported 20 collected cases of sarcoma of the appendix; four of these, including his own case, showed the microscopic findings characteristic of lymphosarcoma. Four apparently authentic cases of lymphosarcoma of the duodenum are cited by Crowther.

Incidence.—In 149,469 admissions to the New York Hospital between 1933 and 1942, 20 cases of lymphosarcoma of the gastro-intestinal tract were observed, the diagnosis in all of these being confirmed by microscopic examination. During the same nine-year period 68 carcinomas of the esophagus, 384 carcinomas of the stomach, 11 malignant lesions of the small intestine, and 568 carcinomas of the large intestine and rectum were encountered. By comparing these figures to those which appear in Table I, the relative frequency of lymphosarcoma in our series may be seen. It is an incidence of one case of lymphosarcoma to every 51 cases of carcinoma, or 1.9 per cent of all malignant lesions of the gastro-intestinal tract. This percentage is considerably higher than that of 0.9 per cent given by Warren and Lulenski, who included in this figure their cases of Hodgkin's disease.

TABLE I

LOCATION OF LYMPHOSARCOMA IN THE GASTRO-INTESTINAL TRACT

Location		No. of Cases
Esophagus		1
Stomach		7
Small intestine:		3
Jejunum	1	
Ileum	2	
Appendix		2
Large intestine:		7
Cecal region	2	
Transverse colon	1	
Sigmoid colon	1	
Rectum	3	
Total		20

In this series there were 13 males and 7 females. The ages ranged from 4.5 to 71 years, 12 of the cases being between the ages of 40 and 60 (Table II). The average age was 43.2 years.

TABLE II

AGE INCIDENCE OF LYMPHOSARCOMA

Age in Years	No. of Cases
0–10	2
10–20	1
20–30	1
30–40	4
40–50	3
50–60	5
60–70	3
70+	1
Total	20

CLINICAL MANIFESTATIONS AND PREOPERATIVE DIAGNOSIS

Esophagus.—The single case (Case 1) of lymphosarcoma of the esophagus occurred in a 62-year-old woman, who was admitted complaining of vomiting for five months, during which time she had noted epigastric pain and burning and the sensation that food stuck in her chest. She had lost 60 pounds in one

year, and had had one tarry stool. There were no significant physical findings except evidence of marked loss of weight. There was nothing in the clinical picture to distinguish this from any other malignant lesion of the lower end of the esophagus.

Laboratory data other than roentgenologic were unremarkable. Blood count and examinations of the stool for occult blood were negative.

Gastro-intestinal roentgenologic series (Fig. 1) showed a filling defect in the cardia of the stomach, with narrowing and irregularity of the lower end of the esophagus and a penetrating defect of the lower border of the tumor. *Roentgenologic Diagnosis:* Carcinoma of esophagus.

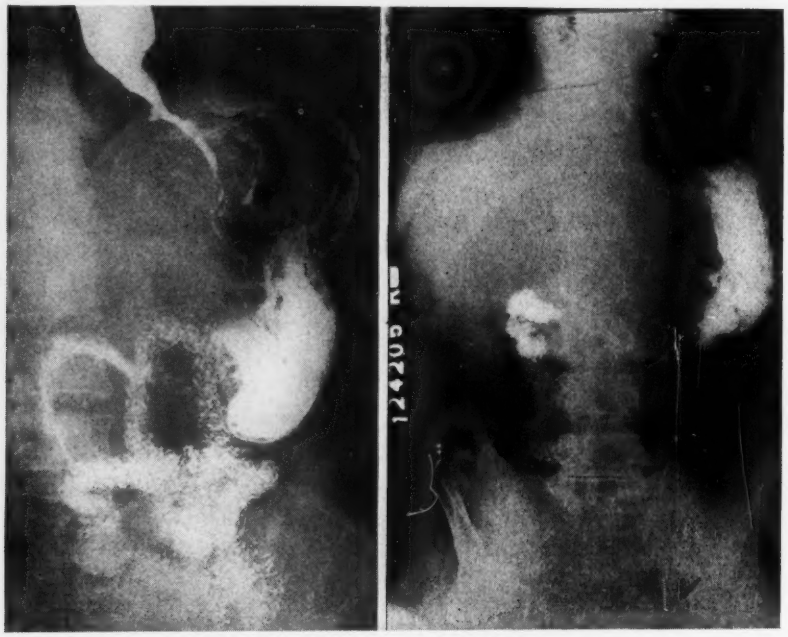

FIG. 1.—Case 1: Roentgenogram showing filling defect in the cardia of the stomach, with narrowing and irregularity of the lower end of the esophagus and a penetrating defect of the lower border of the tumor.

FIG. 2.—Case 8: Roentgenogram showing extensive involvement of the stomach by tumor and typical whorl-like formation along the lesser and greater curvatures in the region of the antrum.

Stomach.—In this group of seven cases there were four females and three males, their ages varying from 43 to 65. The chief complaints elicited were weakness, pallor, anorexia, abdominal pain, "indigestion," nausea and vomiting. The duration of the symptoms varied from 2.5 weeks to 7 months. Six of the seven patients had epigastric pain and five had had vomiting. Three patients had noted tarry stools. There was a history of loss of weight in five patients varying from 9 to 40 pounds. Other symptoms were dysphagia, mass in the upper abdomen, and mass in the right axilla.

Physical examination showed five patients to be afebrile while two had slight fever (38°–38.6° C.). The state of nutrition in four patients was good on admission but there was evidence of loss of weight in three. Only

two had palpable lymph nodes (right axillary in Case 8 and cervical in Case 6). Abdominal examination in four showed the presence of an epigastric mass; in three the mass was slightly tender. Rectal examination revealed an irregular, firm and nontender mass in the cul-de-sac of one patient.

Laboratory findings were of no value in arriving at an accurate diagnosis. Four patients had moderate secondary anemia, the hemoglobin values being 9 to 12 Gm., and the erythrocyte count 3.3 to 3.8 million. The total leukocyte count was normal in all but one, in which it was 13,000; the differential count was normal in all cases. No case of lymphocytosis was observed. The stools were guaiac-positive in five instances. Gastric analysis was performed in six cases; in four there was no fasting free acid, and Case 4 had no free acid after the injection of histamine; the remainder had from 12 to 80 units of free acid.

Two patients were subjected to gastroscopy. In Case 3 a granular area without ulceration was seen on the lesser curvature, and in Case 4 the gastric wall was stenosed and rimmed with tumor. The impression in both was gastric carcinoma.

All patients had gastro-intestinal roentgenograms; a preoperative diagnosis of lymphosarcoma was made in one (Fig. 2, Case 8) and gastric carcinoma in seven. The location of the tumors was as follows: Pylorus, 5 (Cases 3, 4, 5, 6 and 7). Entire stomach, 1 (Case 8). Greater curvature, 1 (Case 2).

In one of the cases in which the lesion was found in the pylorus (Case 3), it also extended up the lesser curvature, where a large crater was observed. In another patient with a pyloric tumor (Case 7), a defective duodenal cap was demonstrated; this patient had an ulcer history of one year's duration.

Small Intestine.—The small intestine was the site of lymphosarcoma in three patients, all of whom were males. In one the lesion was in the jejunum and in the other two in the ileum. All patients had a history of abdominal pain, nausea and vomiting. Two had manifestations of intestinal obstruction. One patient had gross blood in the stool and two had tarry stools. Only one patient had lost weight, in his case 30 pounds in three months.

Physical examination showed increased temperature (38°–39.6° C. in Case 9) before operation in one; the others were afebrile. All patients showed evidence of recent decrease in weight, although only one had given a history of loss of weight. Two had palpable nodes in the cervical, axillary and inguinal regions. Rectal examination was negative in all cases.

One patient had a marked secondary anemia (Case 10, hemoglobin 8 Gm.; erythrocyte count 3.1 million); the other two did not have anemia. The white cell and differential counts were normal in all three instances. The stools of two patients were positive by the benzidine test (Cases 9 and 10).

Roentgenologic studies were made in only two patients. One (Case 10) had a barium enema, which showed a normal colon. A diagnosis of lymphosarcoma was made in one patient (Case 9) by means of a gastro-intestinal series, which showed dilatation of the second portion of the duodenum and proximal portion of the jejunum.

Appendix.—There were two cases of lymphosarcoma involving the appendix; both were females, and their ages were 39 and 47 years.

Their symptoms and physical findings were as follows: One patient had had pain in the right lower quadrant of the abdomen for two days, with nausea and vomiting, and she gave a history of a similar episode six years previously. The physical findings were typical of appendicitis. Her temperature was 39.8° C; she had diffuse rigidity in both lower quadrants and marked tenderness over McBurney's point. No mass was palpated and no tenderness elicited on rectal examination.

The second patient had no symptoms referable to the gastro-intestinal tract. She was admitted to the hospital for bleeding from a fibromyoma of the uterus. A mass was palpable in the left adnexal region. There were no other physical signs of significance.

Neither patient had palpable lymph nodes. Neither roentgenologic studies nor stool examinations were made.

Large Intestine.—Lymphosarcoma of the large intestine occurred in seven patients, all of whom were males with ages ranging from 4.5 to 65 years. The sites were: Cecum (involving appendix and terminal ileum), 2. Transverse colon, 1. Sigmoid colon, 1. Rectum, 3.

The chief complaints were abdominal pain, pruritus ani, constipation, abdominal mass, and rectal bleeding. The duration of symptoms varied from four weeks to four years. Other symptoms were diarrhea, distention, and increased temperature. One patient had had a duodenal ulcer for three years. Abdominal pain was present in four cases, vomiting in only one, symptoms of intestinal obstruction in one, bloody stools in three, and loss of from 9 to 25 pounds in weight in four.

Physical examination revealed that all patients were afebrile on admission. Four showed evidences of loss of weight. In only three patients were there palpable nodes, all of these being in the inguinal region. Abdominal masses were palpable in three instances; epigastric in one, lower right quadrant in one, and lower left quadrant in the third. Abdominal tenderness was present in four patients. Rectal examination in five of the seven cases disclosed the presence of a mass; two of the lesions appearing clinically to be rectal polypi.

Laboratory data showed the presence of secondary anemia in two cases (Cases 13 and 17—hemoglobin 9.6 and 10.2 Gm., respectively). In one case (Case 17) there was a leukocytosis of 21,700, with 58 per cent lymphocytes; this was the patient with a large inoperable tumor of the sigmoid, who later developed metastases in distant nodes. In the other cases the total leukocyte and differential cell counts were within normal limits.

Proctoscopic examinations were made in five of the seven patients, and normal rectal mucosa was found in two. In one, examination showed an ulcerated, fungating lesion 7 cm. above the internal sphincter on the left rectal wall (Case 17), and in another, a reddened mass on the right wall 2 x 3 cm. in size, with a broad pedicle, and no ulceration (Case 20). Case 18

presented a 7-mm. polypus anteriorly about 5 cm. from the anus, and Case 19 had four rectal polypi.

Barium enemas were given in five instances, and showed normal colons in two cases with rectal lesions. In two cases there were filling defects in the cecum; one (Fig. 3) showing an intussusception of the terminal ileum into the ascending colon. In one, a filling defect was demonstrated in the distal transverse colon (Fig. 4) 10 cm. proximal to which a second constricting lesion was seen. The roentgenologic diagnosis was carcinoma in two, lymphosarcoma in one, and intussusception in one case.

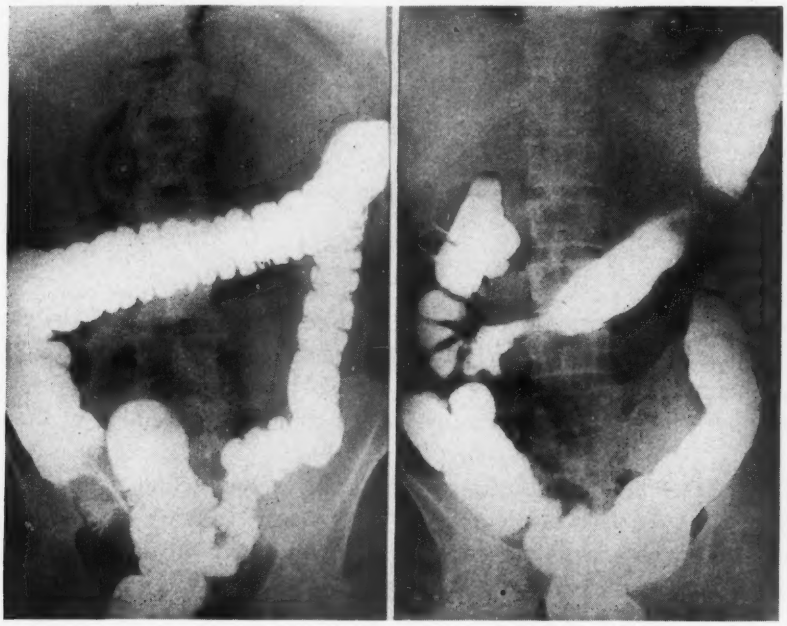

FIG. 3.—Case 12: Barium enema demonstrating intussusception of the terminal ileum into the ascending colon.
FIG. 4.—Case 16: Roentgenogram showing defect in the distal transverse colon and a second constricting lesion proximal to it.

OPERATIVE FINDINGS AND THERAPY

Seventeen operations were performed upon 16 patients, excluding exploratory celiotomies and biopsies. Abdominal explorations and biopsies were undertaken in four cases, excision of a lymph node for microscopic examination once, and proctoscopy and biopsy once (Table III).

Esophagus.—At operation this tumor was found to involve the distal 2.5 cm. of the esophagus, extending to the cardia of the stomach, without demonstrable metastases to the liver or regional lymph nodes.

In this single case (Case 1), exploratory celiotomy and ligation of the left gastric artery was done, followed five days later by resection of the lower esophagus and cardia of the stomach, with esophagogastrostomy by the thoracic approach.

Stomach.—The main regions of involvement by tumor at operation were the lesser curvature in two cases, the greater curvature in two cases, and

TABLE III

OPERATIVE PROCEDURES

Resections:		
Gastric resection:		
Wedge resection	1	
Subtotal resection	5	
Resection of jejunum		1
Appendicectomy		2
Exploration and ligation of left gastric artery		1
Resection lower esophagus, with esophagogastrostomy		1
Excision of rectal polypi		2
Palliative:		
Partial reduction of intussusception		1
Ileo-ileostomy		1
Ileocolostomy		1
Cecostomy		1
Diagnostic:		
Lymph node biopsy		1
Proctoscopy and biopsy		1
Exploratory celiotomy and biopsy		4
Total		23

the antrum and posterior wall in one. In one case two thirds of the stomach was involved, with extension into the abdominal wall. In the remaining case, which was not explored—the diagnosis being made by supraclavicular lymph node biopsy—gastro-intestinal series showed involvement of the entire stomach.

In all cases but one the tumor was large and resection of at least two-thirds of the stomach was necessary in four cases. In none was the diagnosis of lymphosarcoma made at operation. Involvement of the regional nodes was noted in four cases, absent in one, and not mentioned in one. Liver metastases were not present.

One patient was subjected to excision of a supraclavicular lymph node, one to a wedge resection of the stomach, and the other five to subtotal gastric resections.

Jejunum.—In this single case there were three separate lesions, 15 cm. apart, with partial obstruction causing dilatation of the duodenum and proximal jejunum. The operation performed was a resection of the proximal 40 cm. of jejunum, removal of mesenteric nodes, which contained metastases, and lateral anastomosis.

Ileum.—In one case there was a tumor, 45 cm. proximal to the ileocecal valve, obstructing the lumen and involving the mesenteric nodes. An entero-enterostomy and biopsy of lymph nodes was done.

In the second case the lesion lay in the terminal ileum, producing intestinal obstruction. A palliative ileocolostomy was performed.

Appendix.—In one case the appendix contained a wart-like swelling in its middle third; in the other no tumor was noted on gross inspection at operation. Appendicectomy alone was performed in both instances.

Large Intestine.—In one case the cecum, the appendix and the terminal ileum were involved in a hard, nodular mass causing intussusception of the terminal ileum extending as far as the descending colon. Partial reduction of the intussusception was carried out, followed in seven weeks by an exploratory celiotomy which revealed that the lesion was inoperable and biopsy alone was performed. Large retroperitoneal masses were found. A second case, with involvement of the cecum, the appendix and the terminal ileum, had an appendicectomy and biopsy of lymph nodes.

TABLE IV

SUMMARY OF RESULTS OPERATIVE AND ROENTGENOTHERAPY

	No. of Cases		Follow-up Years	Months
Operative and Roentgenotherapy:				
Living without recurrence	2			
Case 5			1	
Case 9			9	5
Living with recurrence	1			
Case 3			3	5
Dead	3			
Case 4			1	10
Case 6				10
Case 7				1
Roentgenotherapy alone:				
Living without recurrence	2			
Case 10			9	6
Case 20			1	8
Living with recurrence	1			
Case 17			4	2
Dead	3			
Case 11			6	
Case 12				4
Case 16				2
Not followed	1			
Case 13				
Operation only:				
Living without recurrence	5			
Case 1			2	4
Case 14			4	3
Case 15			2	2
Case 18			2	4
Case 19			2	2
Living with recurrence	0			
Dead without recurrence	1			
Case 2			7	2
No treatment	1			
Dead				
Case 8				½
Total	20			

The transverse colon was the site of involvement in one case. In the midportion there was an annular, freely movable tumor, 6 cm. in length, with a second similar lesion 15 cm. distal to the first, with infiltration of the gastrocolic ligament and metastases in the liver. Biopsy only was feasible.

In the isolated instance in which the sigmoid was the site of lymphosarcoma, exploratory celiotomy revealed 12 cm. of the sigmoid colon to be shrunken, indurated, and to contain palpable nodules, which were biopsied.

Rectum.—One case had four polypi 7 cm. from the mucocutaneous junction; another had a polypus about 2 cm. above the internal sphincter, and the

third presented a 2 x 3 cm. mass just above the internal sphincter. In the first two patients excision of the rectal polypi was performed and a biopsy taken in the third.

ROENTGENOTHERAPY

Thirteen of the 20 patients were given roentgenotherapy. Two of these (Cases 12 and 16) tolerated radiation so poorly that it was discontinued before the outlined dosage could be given; both of these patients died of fulminating lymphosarcoma. (Table IV)

TABLE V

MICROSCOPIC PATHOLOGY

Microscopic Pathology	No. of Cases	Dead	Alive with Recurrence	Alive without Recurrence
Reticulum cell sarcoma	1	0	1	0
Large cell lymphosarcoma	4	3 (or 4*)	?*	
Small cell lymphosarcoma	12	4	0	8
Giant follicle sarcoma	3	1	1	1

*Case 13 not followed.

Six of the patients were subjected to resection of the tumor followed by prophylactic roentgenotherapy. Case 7 died of postoperative hemorrhage 33 days following gastric resection, after having received 330 r. through three upper abdominal portals. Three patients received roentgenotherapy in addition to palliative procedures, four received roentgenotherapy alone and in six resection only was performed.

In all instances that tolerated the therapy the response to the roentgen-ray was good as far as the local lesion was concerned. Palpable masses often melted away dramatically following irradiation. One patient with involvement of the cecum received 700 r. through four portals to the right abdominal mass, which diminished in size but rapidly became larger when the therapy had to be discontinued because the patient developed marked anemia and leukopenia.

In this small series of cases the prognosis was better in the small cell lymphosarcoma than in the other types of tumor (Table V). The roentgen-ray dosage varied considerably over the period of nine years but, in general, amounted to from 1400 to 2000 r. directed at the region involved through two to four portals.

PATHOLOGY

Gross Pathology.—In general, lymphosarcoma arises in the submucous layers of the intestinal tract and infiltrates the surrounding tissues. Usually all of the layers of the intestinal tract except the serosa are invaded but in two cases there was extension through the serosal surface of the stomach and invasion of the anterior abdominal wall. Involvement of regional nodes occurs frequently and was present in 12 cases in this series.

At operation, the gross appearance of lymphosarcoma differs sufficiently

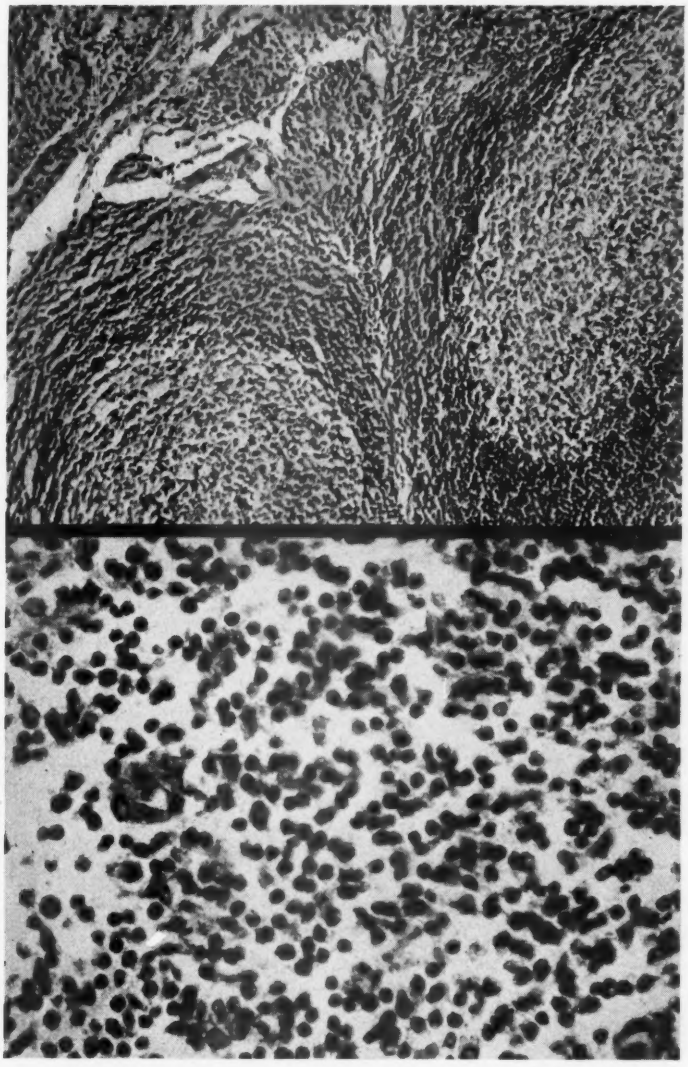

FIG. 5.—Case 17: (Sigmoid) Photomicrograph showing enlarged lymph follicles characteristic of giant follicle lymphosarcoma. (× 150)
FIG. 6:—Case 1: (Esophagus) Photomicrograph showing uniform small lymphocytes and scant stroma in a small cell lymphosarcoma. (× 600)

from that of carcinoma to be identified or suspected at operation. The lymphosarcomatous mass usually is firm but softer than the hard consistency of carcinoma; it is friable, often rubbery and nodular, and the cut-surface resembles the whitish-grey homogenous appearance of lymphoid tissue. Ulceration is frequent and occurred in at least five of the cases reported.

Microscopic Pathology.—The tumors in this series were classified as (1) nodular lymphosarcoma; (2) small round cell lymphosarcoma; (3) large round cell lymphosarcoma; and (4) reticulum cell lymphosarcoma. Nodular lymphosarcoma (giant folliculoma or Brill-Symmer's disease, Fig. 5) is characterized by enlargement of the lymph follicles, composed of cells with

large vesicular nuclei and showing numerous mitoses; they should not show phagocytosis. The large and small cell lymphosarcomas (Figs. 6, 7 and 8) both show disruption of the normal lymph node architecture, invasion of the capsule, numerous mitoses, with predominance, on the one hand, of the

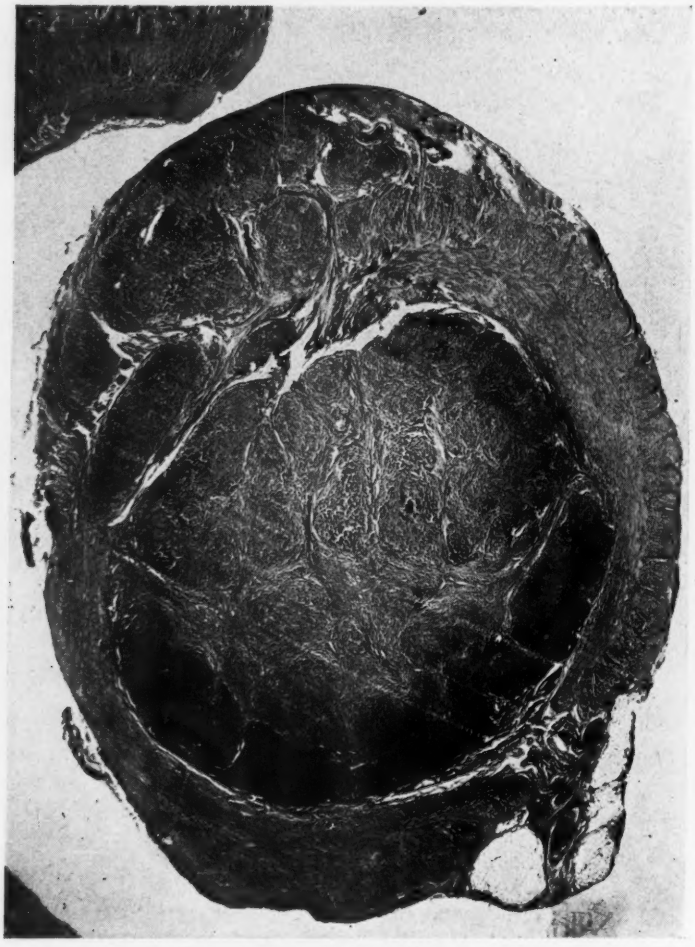

FIG. 7.—Case 15: (Appendix) Cross-section of lumen filled with large lymphoid follicles which replace the mucosa and submucosa of the appendix. (× 10)

large lymphoblast and, on the other, of the small lymphocyte. Usually the struma is scanty. Reticulum cell sarcoma (Fig. 9) is recognized by the sheets of cells, often crescentic, tailed or polyhedral in shape, with large clear nuclei; by the loss of the normal lymph node architecture and the demonstration of the characteristic reticulum fibers by special stains (notably the method of silver impregnation of Foot and Foot).

The relation of histologic pattern to survival time is illustrated in Tables V and VI.

All cases were reviewed by Dr. N. C. Foot, with the authors, and were verified by him as being lymphosarcoma of the groups as classified above.

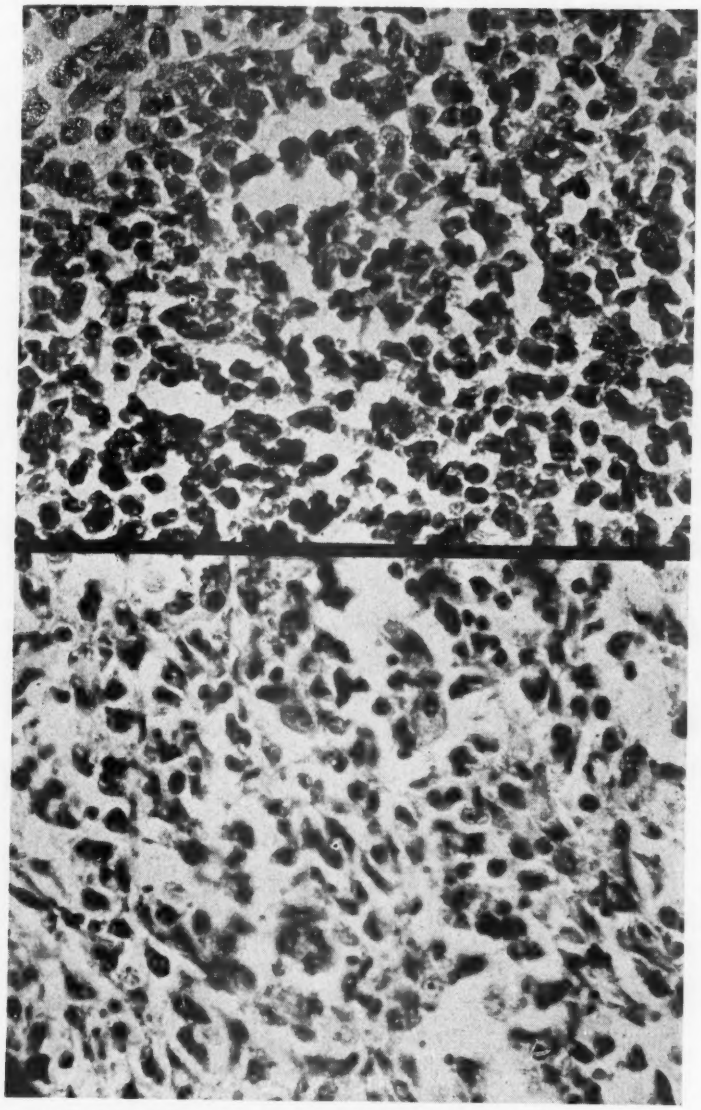

FIG. 8.—Case 9: (Jejunum) Photomicrograph showing uniform large lymphoblasts with numerous mitoses and scant stroma. (× 600)
FIG. 9.—Case 3: (Stomach) Photomicrograph of reticulum cell sarcoma demonstrating large reticulum cells with tailed and polyhedral cells. (× 600)

DISCUSSION.—*Diagnosis:* A diagnosis of lymphosarcoma of the gastro-intestinal tract seldom is made before histologic examination, due to the fact that the signs and symptoms produced by this type of malignant growth are little different from those caused by other gastro-intestinal neoplasms.

Although there is nothing specific in the clinical manifestations of these patients which might lead to a diagnosis of lymphosarcoma, the appearance of the mass soon after the onset of symptoms is suggestive of this type of tumor, as is a large mass in a patient in good general condition.[14]

A roentgenologic diagnosis of lymphosarcoma was made in only three cases in this series. It is difficult to differentiate lymphosarcoma by roentgenologic examination because the picture so closely resembles that of carcinoma; however, there are diagnostic points which suggest lymphosarcoma; *i.e.*, (1) the large size of the lesion in relation to the short duration of symptoms;[14] and (2) the presence of whorl-like defects in the barium outline (Figs. 2 and 10). In the diagnosis of neoplasms of the colon, a double or

FIG. 10.—Case 5: Roentgenogram of stomach showing whorl-like defects along the greater curvature.

an usually long mass is suggestive of lymphosarcoma. Tuberculous colitis and regional colitis must be ruled out before this diagnosis is made. When the above characteristics are present, the diagnosis of lymphosarcoma should be made; unfortunately, however, these roentgenologic findings often are absent and consequently the preoperative diagnosis usually is carcinoma.

Blood counts were throughout of no aid in diagnosis, the count having been unusual in only one case.

RESULTS OF TREATMENT

The survival of the patient is influenced more by the site and extent of the growth than by the histologic type of neoplasm or the age of the patient. The prognosis largely depends upon whether the lymphosarcoma is localized and can be treated as an isolated lesion, or whether a general spread has occurred.

The six patients in whom the lesion was sufficiently localized to allow extirpation, have survived from two to seven years without receiving roentgenotherapy. The location of these tumors was strikingly varied, involving as they did the esophagus, stomach, appendix and rectum. However, in all six cases the tumor was well-localized and without apparent lymph node involvement. One of these patients died later of an unrelated condition, without evidence of recurrence.

Of the six patients treated with roentgenotherapy alone, only two (Cases 10 and 20) are without evidence of recurrence. In two cases (Cases 5 and 9) resection of the lesion was followed by irradiation without evidence of a return of tumor. In four, resection followed by irradiation gave poor results. In one case (Case 6) irradiation was started five months after operation, obviously too late for maximum prophylactic value; Case 16 tolerated the therapy so poorly that it was discontinued. Case 4 had a large lesion originally and had recurrences involving the left inguinal and iliac chains of nodes. Still later she developed a large cutaneous mass in the left posterior thoracic region and shortly thereafter she expired. In general, the appearance of subcutaneous masses or nodules in lymphosarcoma is of grave prognostic significance. In contradiction to reports by some observers[15, 16] the reticulum cell sarcoma in this series was quite radiosensitive. The patient who had this type of tumor had had several recurrences over a period of three years; each time the tumor melted away rapidly after roentgenotherapy.

Nine patients are alive and without recurrence at present; their original tumors were located in the esophagus, stomach, jejunum, ileum, appendix (two) and rectum (three). One case of lymphosarcoma of the stomach died seven years and two months after operation from hypertensive cardiovascular disease, without evidence of recurrence.

SUMMARY

A series of 20 cases of microscopically proven lymphosarcoma of the gastro-intestinal tract is presented—the lesion having arisen in all areas of the gastro-intestinal tract except the duodenum.

The clinical manifestations, laboratory, roentgenologic and operative findings are reviewed and the treatment by operation and irradiation described.

Cures of five or more years were obtained after roentgenotherapy alone in one case (Case 10), after surgical extirpation in one (Case 2), and after a combination of the two in one (Case 9). Nine cases (47 per cent of cases followed) are alive and well at present, without evidence of recurrence from one year to nine years and five months since the diagnosis was established.

The mortality at the present state of follow-up is 42 per cent (8 of the 19 cases followed). From the time of establishment of the diagnosis in eight patients who died, the average duration of life was 24 months. The average for the entire series (including those now alive) was 37 months. The latter figure is of little importance because of the short period of time which has elapsed in six patients since the establishment of the diagnosis.

CONCLUSIONS

Lymphosarcoma may be found at any point in the gastro-intestinal tract, including the appendix.

The preoperative diagnosis of lymphosarcoma of the gastro-intestinal tract is rarely made.

The prognosis is most favorable in instances suitable for complete extirpation, and we think that resection should be undertaken, if technically possible, although in this small series of cases the duration of life was apparently shorter following a combination of resection and roentgenotherapy (11 months for three patients who died, 33 months for six patients, including three still living) than after roentgenotherapy alone (26 months for three patients who died, 44 months for six patients, including three living). Roentgenotherapy alone occasionally results in apparent cure.

Roentgenotherapy should be given in every case of lymphosarcoma of the gastro-intestinal tract unless the operator and surgical pathologist are certain that the lesion has been completely eradicated. Irradiation should be started as soon as the wound is healed and the patient is ambulatory.

We are indebted to Dr. John L. Sullivan and Dr. Harold Temple of the Roentgenologic Department of the New York Hospital, and to Dr. N. C. Foot of the Department of Surgical Pathology for their valuable suggestions and advice.

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HYPERTROPHIC PYLORIC STENOSIS IN ADULTS

REPORT OF TWO CASES

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HYPERTROPHIC PYLORIC STENOSIS of infancy is a well recognized disease entity. It is not fully appreciated, however, that the same condition may be found in adults as well. Some one hundred odd cases of simple pyloric muscle hypertrophy in adults have been reported in the literature[1] and, no doubt, numerous other unrecorded cases have been encountered. Our sum total of knowledge regarding this peculiar condition as it occurs in adults is meager indeed. The etiology of the disease is still obscure despite a host of speculative theories; the clinical features show a wide variation and there is no uniformity in the method of management. For these reasons we considered it would be of value to report two cases of simple hypertrophic pyloric stenosis in adults which we have recently studied. Not only do these cases serve to call attention to the condition, but they also are of interest because of the possibility in each that psychogenic factors played an important etiologic rôle.

CASE REPORTS

Case 1.—M. E. P., white, male, age 39, first experienced inconsistent, dull, gnawing epigastric pain in 1937. This tended to appear about two hours after meals, was commonly associated with vomiting, and was alleviated by the ingestion of milk or soda. The initial episode lasted about one week and then spontaneously disappeared. Subsequently, there occurred similar attacks of some two to three weeks' duration, the last of which was in 1940. Though married and with a daughter of about 15 years of age, his married life was unpleasant and disruptive. His livelihood was earned from commissions made in his capacity as a traveling salesman. In latter years he had acquired a mistress, and it became necessary for him to increase his earnings in order to support her as well as his family. As a consequence, he redoubled his efforts at selling, tending to work harder, longer, and with greater zeal. On several occasions when he was about to clinch an important sale he was conscious of becoming exceedingly tense and tremulous. It was common for him at these times to experience epigastric pain entirely similar to that which had been recurring in attacks since 1937.

He performed his duties in the army without any digestive difficulty from the time of his induction in June, 1942, until early February, 1943. During the latter period epigastric distress reappeared along with vomiting and he was required to seek hospitalization. After appropriate study a diagnosis of gastric ulcer was made and, on April 1, 1943, he was transferred to Tilton General Hospital.

On admission, he was ambulatory and in no acute distress. Physical examination was essentially negative except for some epigastric tenderness. Blood studies, including red and white cell counts, urea nitrogen, chlorides, total protein, albumin and globulin values were all within normal limits. The Wassermann and Kahn tests were negative. Fractional gastric analysis with an Ewald meal showed a maximum free acid of 8 and a maximum total acidity of 30 clinical units; impairment in motor function of the

FIG. 1

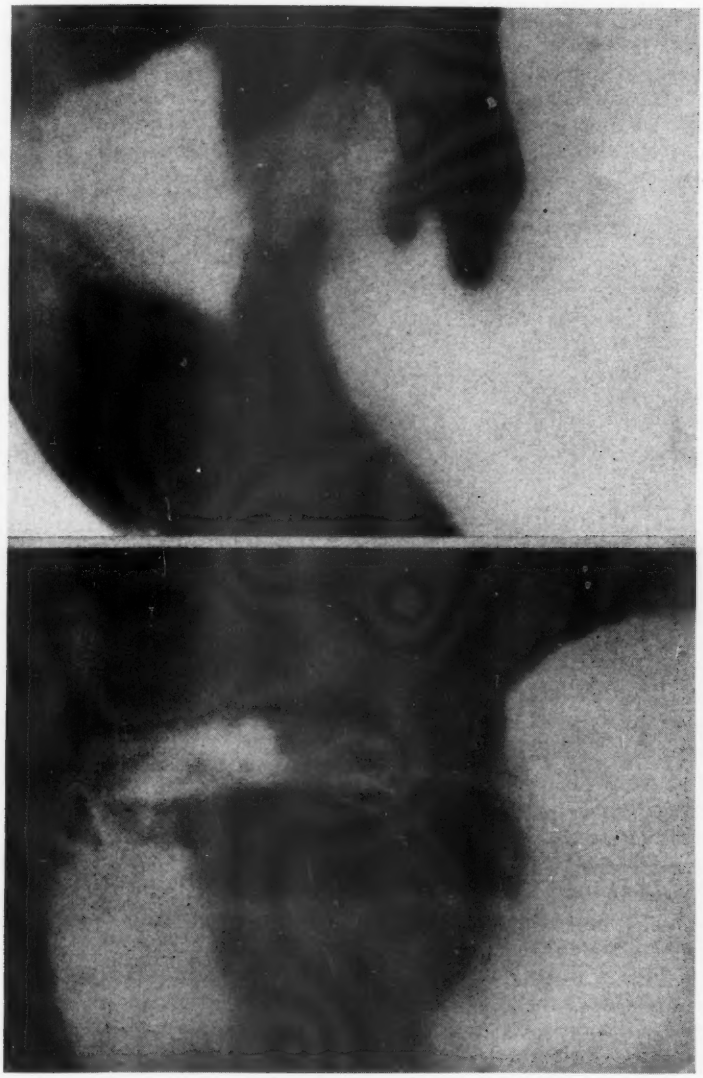

FIG. 2

FIG. 1.—Case 1: Roentgenogram showing narrowing of the pars pylorica. Note smooth and regular contour of the stomach at the antral extremity of the narrowed area.

FIG. 2.—Case 1: One of a serial roentgenogram showing, again, the marked narrowing of the pars pylorica. Note regular straight folds indicating absence of mucosal involvement.

stomach was indicated by some delay in emptying of the test meal. Gastroscopy revealed a normal appearing mucosa. Roentgenologic examination of the stomach and duodenum disclosed a persistent narrowing of the distal end of the stomach. This area was tubular in character and peristalsis did not pass through it. At the lower extremity of the narrowed area, on its lesser curvature side, was a persistent double incisura with an interposed teat-like projection (Fig. 1). The walls of the antrum appeared thickened and could not be distended on forced filling. Despite the narrowing and irregularity of the pars pylorica, the mucosa in this region appeared to be intact (Fig. 2). The radiopaque meal readily passed through the pylorus and at the end of six hours the stomach was completely empty. These findings were interpreted as indicative of either a constricting type of malignant infiltration or a benign juxta-pyloric ulcer associated with spasm and cicatrization.

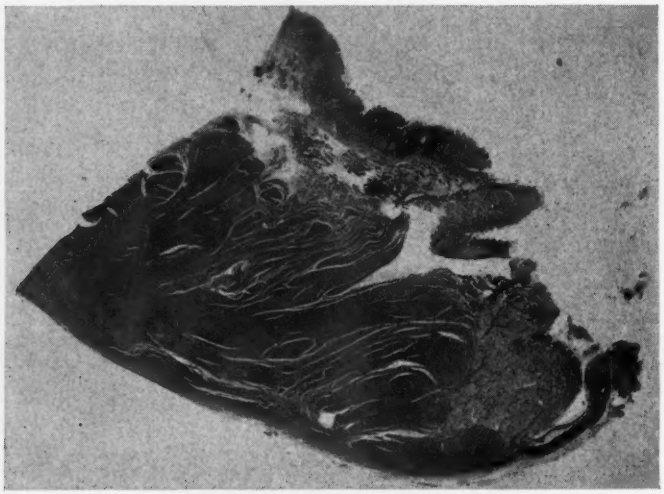

FIG. 3.—Case 1: Histopathologic section of the gastroduodenal junction showing marked hypertrophy of the muscularis of the pars pylorica.

On a rigid ulcer regimen the patient remained asymptomatic, and even gained some five pounds in weight. However, roentgenologic reexamination after three weeks of this program showed no change in the appearance of the antrum. In view of his age, the hypoacidity, and the roentgenologic findings, it was felt that malignant infiltration could not be excluded other than by surgical exploration. Accordingly, May 4, 1943, a celiotomy was performed under general anesthesia. The stomach was found to be normal except for moderate thickening and induration of the pars pylorica; the duodenum was normal; no enlarged lymph nodes were found, and no lesions indicative of metastatic malignancy could be identified in the liver or other adjacent structures. Since a neoplasm of the stomach could not be definitely excluded on the basis of inspection and palpation alone, a subtotal antecolic Pólya-type of gastric resection was performed.

Histopathologic Examination.—Gross: "The specimen consists of the distal segment of the stomach. The pyloric ring measures 5 cm. in circumference and the line of section measures 15 cm. in circumference. The lesser curvature measures 4.5 cm. and the greater curvature 9 cm. There are large dilated veins seen on the serosa along the lesser curvature. The mucosa along the lesser curvature, extending from the anterior to the posterior walls, appears granular, reddened, and thickened. There are several small scattered mucosal hemorrhages. The muscle in the pylorus shows considerable increase in size in all dimensions. It forms a wide, thick, garter-like band, which is

2 cm. in width and 0.6 cm. in thickness. The adjacent stomach musculature is also somewhat thickened. The muscle bundles are translucent and glistening and are separated by white firm connective tissue.

"Microscopic Examination. A—Pylorus: Marked congestion with small hemorrhages and some edema is present in the epithelium of the pyloric mucosa. There is a large submucosal hemorrhage. A cellular infiltration exists throughout the mucosa, the predominant cell being the plasma cell, but there are also a moderate number of eosinophils and polymorphonuclear leukocytes. There is some edema between the acini.

"Examination of the pyloric musculature reveals it to be thickened (Fig. 3). The smooth muscle forms a large wide oval area composed of bundles of muscle which have apparently undergone both hyperplasia and hypertrophy. There is a small amount of connective tissue separating some of the muscle bundles, but the predominating tissue is muscle.

"B—Granular Area on the Lesser Curvature: The muscularis is moderately thickened. In the mucosa, there is a marked congestion of capillaries along with a moderate number of polymorphonuclear leukocytes and a few eosinophils. Several lymphoid follicles are present, the germinal centers of which show moderate hyperplasia. The tissue in the submucosa is edematous and of a loose areolar character. Scattered throughout this area are numerous lymphocytes and a few polymorphonuclear leukocytes and eosinophils. There is a marked congestion of the serosa with scattered hemorrhages in the serosal fat. An occasional small artery in the serosa shows marked obliterative changes; some perivascular focal collections of lymphocytes are present.

"C—Prepyloric Region: Diffuse infiltrations of plasma cells with some polymorphonuclear leukocytes and eosinophils are seen. Some lymphoid follicles show hyperplasia of the centers. The submucosal tissue is loose and areolar.

"D—Distal Line of Resection: The changes here are similar to those described in the above sections.

"Pathologic Diagnoses: 1. Hypertrophic pyloric stenosis. 2. Chronic gastritis, nonspecific. 3. Hypertrophy of the muscularis of the antrum, moderate."

Subsequent Course.—The postoperative course was without complication except for some pain and weakness in the left arm, which the patient attributed to intravenous therapy he had received. This complaint afforded us further insight into the personality of the patient and will be described in more detail later. Roentgenologic examination on June 1, 1943, revealed no abnormalities in the remnant of the stomach or in the anastomotic area; the ostium functioned well, and at the end of three hours only a trace of the radiopaque meal remained in the stomach. Fractional gastric analysis, June 2, 1943, showed an achlorhydria both to an Ewald meal and to histamine. Gastroscopic examination, June 8, 1943, disclosed a patent gastrojejunostomy, without any evidence of mucosal changes in the remnant of the stomach. The patient remained symptom-free, and was discharged from the hospital, July 1, 1943, in excellent condition.

Case 2.—J. T. O., white, male, age 37, was inducted into the army in January, 1943. For many years he had been compelled to follow one type of employment during the day, and another by night, in order to support his seven children and pay for the cost of institutional care for his wife, who was an inveterate drunkard and whose behavior was a constant source of embarrassment and concern to the patient. He volunteered the information that abdominal distress would be experienced at times when his social difficulties were particularly trying. The discomfort was usually of very short duration and he gave it little thought. In the early part of February, 1943, he began to experience regularly recurring, upper abdominal discomfort characterized, in the main, by a sensation of fullness after eating. The postprandial distress varied in intensity, was intermittent, and was relieved by vomiting. At times there was a burning sensation in the epigastrium associated with sour eructations. These would be alleviated by the ingestion of milk or aluminum hydroxide gel. Symptoms recurred almost daily throughout March, being worse after the midday meal and two to three

hours after the evening meal. His appetite remained good, but he had lost about 15 pounds in weight. There was no severe pain, hematemesis or melena. Since the onset of his present illness it was apparent to him that his symptoms were decidedly aggravated by episodes of worry and strife. In April, 1943, he was forced to seek medical aid despite his disinclination to do so. Evidence was found of pyloric obstruction and, May 21, 1943, he was transferred to Tilton General Hospital.

On admission, he was ambulatory and in no acute distress. A moderate degree of undernourishment was apparent. Enlargement of the stomach, with a loud succussion splash, could be elicited on abdominal examination; peristalsis was not visible and no masses could be felt. Blood studies, including red and white cell counts, urea nitrogen, chlorides, carbon dioxide combining power, total protein and albumin and globulin values were all within normal limits. The Wassermann and Kahn tests were both negative. An overnight retention of food, with a fasting residuum of 500 cc., was found in the stomach. The free acid of the contents of the fasting stomach measured 25 and the total acidity 58 clinical units. On fractional gastric analysis no free acid was exhibited in response to an Ewald meal, but after histamine a maximum free acid of 27 and a maximum total acidity of 55 clinical units was obtained. Gastroscopic examination showed some distortion in the anatomic alignment of the distal antrum; the pylorus could not be seen, and there was no evidence of gastritis. Roentgenologic studies of the stomach and duodenum, May 25, 1943, disclosed an hypotonic, slightly enlarged stomach. The contents of the fasting stomach had been evacuated by tube just prior to the roentgenologic examination, yet nonopaque material was found in the stomach at the time of examination. The pylorus was markedly narrowed and in the pyloric canal a persistent niche was noted (Fig. 4). A conspicuous finding was a marked indentation of the base of the duodenal bulb which was accentuated even more in the compression films (Fig. 5). Six hours after its ingestion about 60 per cent of the opaque meal was still retained in the stomach. The changes observed were interpreted as due to pyloric obstruction and thickening secondary to pyloric ulcer.

A rigidly enforced stomach-rest regimen was instituted. After almost three weeks of this program the pyloric obstruction, both clinically and roentgenologically, was essentially unchanged, even though the patient was rendered symptom-free. The failure of the pyloric obstruction to show any satisfactory response to a rigid medical regimen during this period of time was felt to warrant surgical intervention. Accordingly, June 14, 1943, a celiotomy was performed, under continuous spinal anesthesia. The stomach was found to be a little dilated and at its pyloric extremity a firm thickening could be felt. There was no evidence of ulcer scarring and no undue enlargement of the adjoining lymph nodes. No metastatic lesions could be made out in the adjacent structures. In view of the more or less complete obstruction, and since the nature of the pyloric mass could not be determined with certainty by inspection and palpation alone, a subtotal antecolic Pólya-type of gastric resection was performed.

Histopathologic Examination.—Gross: "The specimen consists of the distal portion of the stomach. The serosa is congested. It is difficult to force the small finger through the pylorus. The mucosa of the antrum is coarsely granular and the rugal folds appear hypertrophic. The mucosa of the pylorus is smooth and atrophic. The pyloric muscle measures 2 x 1 cm. On cross-section it appears to be increased in density. The entire wall of the stomach appears thickened.

"Microscopic Examination. A—Pylorus: The mucosa appears to be somewhat thicker than might normally be expected. Numerous leukocytes are present in the interstitium and some of the glands are separated by this cellular deposit. There are numerous lymphocytes and many plasma cells; occasional eosinophils and polymorphonuclear leukocytes are also seen. There is some increased vascularity in the submucosa. Occasional thick-walled blood vessels are present. The muscularis is converted into a large broad band in which numerous bundles of smooth muscle are

FIG. 4

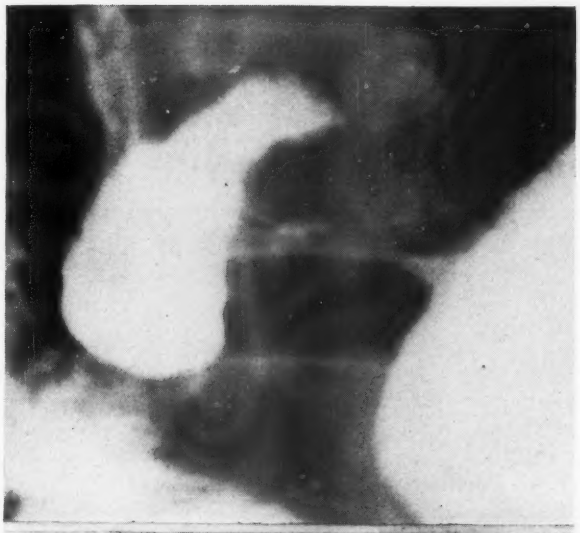

FIG. 5

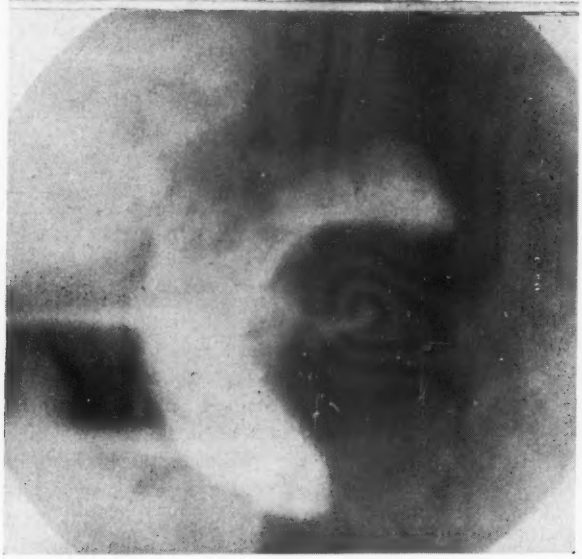

FIG. 4.—Case 2: Roentgenogram showing extreme narrowing of the pars pylorica. The contour of the stomach at the proximal limit of the narrowed area is smooth and regular. A "fleck" of barium is seen just proximal to the base of the duodenal cap. Note invagination of the base of the duodenal bulb.

FIG. 5.—Case 2: Roentgenogram taken with compression over the duodenal cap showing in striking fashion the smooth concave deformity in the base of the latter.

present (Fig. 6). These muscles have undergone both hypertrophy and hyperplasia. Some collagenous connective tissue is present between the muscle bundles.

"*B—Antrum:* Mucosal changes are revealed which are similar to those described above. Occasional small lymphoid follicles are seen in the mucosa. The muscularis mucosa is prominent. The submucosa shows an increased vascularity. The muscularis also seems to have undergone some hypertrophy and hyperplasia, but this is less marked than at the pyloric ring.

"*C—Body:* Mucosal changes similar to those above described are seen. However, there seems to be more edema in the mucosa and somewhat less cellularity. The muscularis is also somewhat increased in dimension.

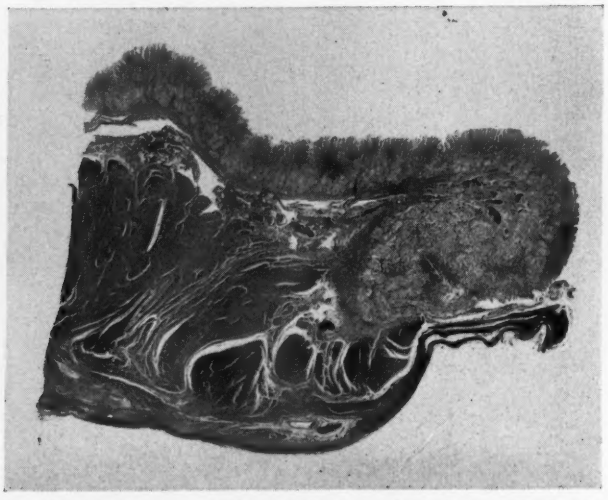

FIG. 6.—Case 2: Histopathologic section of gastroduodenal junction. Note striking difference in thickness of the muscularis between that of the pars pylorica and that of the adjacent duodenum.

"*Pathologic Diagnoses:* 1. Hypertrophic pyloric stenosis. 2. Gastritis, chronic, nonspecific. 3. Hypertrophy of the muscularis of the antrum, moderate."

Subsequent Course.—The postoperative course was entirely uneventful and without complication. Fractional gastric analysis, July 7, 1943, disclosed an achlorhydria both to an Ewald meal and to histamine. Roentgenologic examination, July 8, 1943, showed no abnormalities in the remnant of the stomach or in the anastomotic area; at the end of three hours only about 10 per cent of the radiopaque meal was still in the stomach. Gastroscopic examination, July 17, 1943, showed a patent gastrojejunostomy and mild superficial gastritis involving the mucosa immediately proximal to the stoma. The patient remained asymptomatic and was discharged from the hospital, August 7, 1943, after having gained 12 pounds in weight.

COMMENT.—Hypertrophic pyloric stenosis as it is encountered in infants (Fig. 8). exists, as a rule, in the absence of any other organic disease at or near the pylorus. The discovery of gastritis or ulcer ought to exclude the diagnosis of simple pyloric muscle hypertrophy as the primary disease. Yet, such lesions have been described as associates of simple pyloric muscle hypertrophy in adults. In 60 per cent of the 81 cases reported by Kirklin and Harris,[2] organic lesions of the stomach or duodenum, cholecystitis, or appendiceal disease were found in addition to the pyloric muscle hypertrophy.

Although gastroscopic examination prior to operation in both our patients revealed no mucosal abnormalities, chronic gastritis manifested principally by infiltration by plasma and other inflammatory cells, was found on histologic examination of the resected stomachs. The precise relationship between the chronic gastritis and the muscle thickening cannot be stated with certainty. Chronic gastritis may be accompanied by thickening of the pyloric musculature, but this is not often remarkable. On the other hand, the stenosis, particularly the pronounced obstruction seen in Case 2, conceivably, could have resulted

FIG. 7

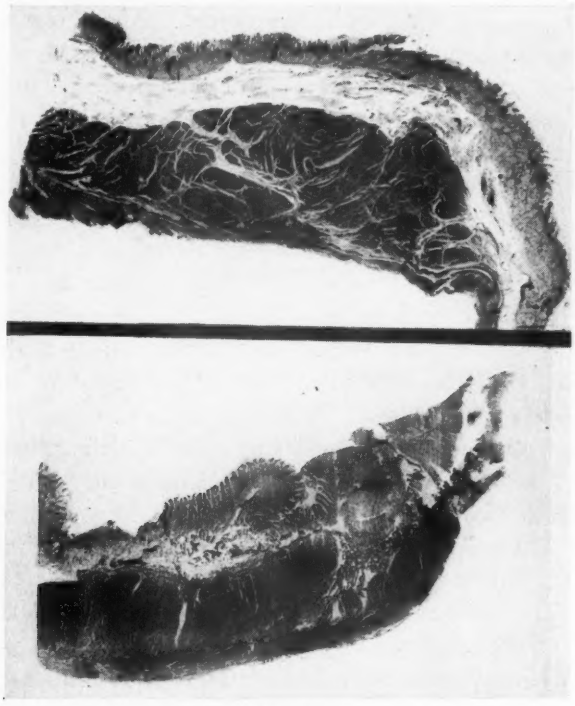

FIG. 8

FIG. 7.—Histologic appearance of normal adult gastroduodenal junction. Note thickness of antral and pyloric musculature in this area as compared with that in Figures 3 and 6.

FIG. 8.—Histopathologic appearance of gastroduodenal junction in a child with hypertrophic pyloric stenosis. (Courtesy of Dr. Walter E. Lee)

in secondary inflammatory changes in the mucosa and submucosa of the stomach at and just proximal to the stenotic area. We feel it justifiable to assume, therefore, that the chronic gastritis found in our cases was not a significant etiologic factor.

From the standpoint of etiology and pathogenesis, the personality pattern that characterized each of our patients is of great importance. Unfortunately, no detailed personality studies were made. The available data, though meager, were, nevertheless, suggestive. Both individuals were aggressive, ambitious, and driving, and both were beset by social and financial problems. When

confronted by distressing situations which would be expected to arouse in any individual a natural reaction of concern and anxiety, both of them were conscious of somatic distress. The pending consummation of a sale or the chagrin and worry occasioned by the responsibility for a wife who was an habitual and inveterate drunkard, are justifiable causes for anxiety in anyone. The fact that both our patients consciously experienced abdominal distress at such times suggests that they were each so constituted that their personality dysfunctioning tended to express itself in a somatic derangement. The latter is further supported by the episode occurring in the period of convalescence of Case 1. He had received several intravenous injections of various types of fluids in the immediate postoperative period. About one week after the last of these he complained of momentary, but severe, twinges of pain in the midsection of his left forearm. He also described a constant burning pain just under the skin in a small circumscribed area around the radial border of the midforearm. The pain was precipitated by motion, complete extension of the elbow, and by pressure in the antecubital fossa. In addition, his arm felt weak and he had no strength in his fist. Thorough examination failed to reveal any objective evidence to indicate an organic nervous lesion and it was the neuropsychiatrist's impression that the pain and weakness were explainable as psychogenic superimpositions. A confident, reassuring manner was adopted and it was pointed out to the patient that his discharge from the hospital could be effected only when the pain and weakness in his arm had completely disappeared. Within a day improvement was apparent; after a few days all pain and distress was gone and the arm was as strong as ever. Proof is lacking, and no certain claim is made, but it is reasonable to hypothecate that prolonged and recurring pylorospasm associated with the personality malfunctionings in each of our patients may have eventuated, at long last, in a fixed hypertrophy and thickening of the pyloric and antral musculature. The validity of this assumption remains to be determined. The existence of a pathogenetic mechanism involving pylorospasm incident to personality dysfunction which, in some cases, may result in a fixed hypertrophy of the pyloric muscle is at least worthy of further consideration. Through the use of extensive personality studies in other such cases, light may be shed on this interesting but insufficiently explored possibility.

Both our patients fall into that group of individuals with hypertrophic pyloric stenosis who, in middle or late life, present a comparatively brief ulcer-like history occurring in conjunction with symptoms and signs of partial to complete pyloric obstruction. In both instances our preoperative considerations favored an obstructing pyloric ulcer, but we were unable to exclude a malignant affection with absolute certainty. Pyloric muscle hypertrophy was considered among the diagnostic possibilities prior to operation, particularly because the narrowed antrum and pylorus with intact mucosa and the invaginated base of the duodenal cap were in keeping with the roentgenographic signs described as distinctive for hypertrophy of the pyloric muscle in adults by Kirklin and Harris.[2] The condition was dismissed from consideration,

however, not only because we felt that it was exceedingly rare, but also because the roentgenograms showed additional irregularities in the antrum which tended to favor other more common lesions.

We elected to perform a subtotal gastric resection in both our cases because of the identification at operation of a pyloric mass, the precise nature of which we could not be certain. In a number of the cases recorded in the literature as instances of hypertrophic pyloric stenosis in adults, the diagnosis was founded merely on the surgeon's observations and was not supported by confirmatory biopsy evidence. In such instances, simple gastro-enterostomy, muscle-splitting, and kindred plastic operations were undertaken. In our opinion, complete reliance for diagnosis on the operative findings alone is a practice fraught with danger. The inability to exclude a malignant growth in these cases justifies, we feel, gastric resection rather than a simple palliative procedure even though one may strongly suspect that the tumor mass is composed only of hypertrophied pyloric muscle.

SUMMARY AND CONCLUSIONS

1. Hypertrophic pyloric stenosis occurs in adults more often than is generally suspected. Two cases seen within a period of two months are reported.

2. The symptom-picture may closely simulate that of peptic ulcer and may develop in middle life without any previous symptoms. Pyloric obstruction of variable degree is a feature.

3. Pyloric muscle hypertrophy in adults may be associated with histologic evidence of chronic gastritis. The exact relationship between the chronic gastritis and the muscle thickening is uncertain.

4. The inability to exclude a malignant growth justifies gastric resection as the procedure of choice.

5. There is suggestive evidence in the two cases reported that prolonged and persistent pylorospasm associated with personality dysfunctioning may have eventuated in hypertrophy of the pyloric musculature.

We are indebted to Major Solomon Weintraub and Captain Joseph Mendeloff for the histopathologic studies; to Major Marston T. Woodruff, Captain John D. Osmond, and Lieutenant Frederick B. Strauss for the roentgenologic examinations; and to Captain Earl Saxe for the neuropsychiatric evaluation of these patients.

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EXPERIENCES IN WAR SURGERY IN CHINA*

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WAR SURGERY must adapt itself to varying conditions and those which prevail in one land may differ from those prevalent in another. Thus, as pointed out by Prof. Seymour Barling,[1] conditions which obtained in the wars in South Africa (1899–1902) and Abyssinia (1941–1942) apparently differed sufficiently from those which obtained in fighting in France and Belgium (1914–1918, 1939–1942) as to warrant a more conservative attitude toward wound excision in the former as compared to the more radical attitude adopted for the latter. Nevertheless, much that we have experienced in war surgery on both sides of the lines in several locations in North China (1938–1941) is applicable in a measure to war surgery elsewhere; if not directly, at least indirectly by contrast and comparison.

Preoperative Measures.—We have reported the preoperative measures, which we employed, elsewhere.[2, 3] Briefly, these consisted in intravenous saline and glucose (used with discretion, no blood nor plasma being available), rest, protein-rich diet, ascorbic acid, sulfonamides, specific treatment for intercurrent disease (particularly malaria), and the delimiting tourniquet. The latter consists of a very tight tourniquet applied to an extremity proximal to a gangrenous area where the patient's condition is so grave that amputation is going to be required eventually. Our experience taught us that preoperative preparation of the patient is very important in war surgery.

Cleansing and Excision of War Wounds.—As to the general treatment of war wounds, soap and water early became our mainstay in cleaning up war wounds. We felt it was far more efficient than any other antiseptic, regardless of color. Although a bit messy, this was easily coped with, once our staff got used to it.

In the case of high velocity gunshot wounds, conservatism seemed warranted, particularly in the dry climate of North China. We are inclined to consider the dryness of the climate with its abundance of sunshine as responsible for a probable reduction of the number of pathogenic bacteria in the clothing, on the skin and in the surrounding environment, for similar deductions on this basis have been made by Weddell.[4] We did not excise these wounds, when perforating and uncomplicated, aside from excising the skin about the wounds of entry and exit in some instances. A clean dressing was applied and the part immobilized. Excision of badly contaminated wounds from bombs and the like, however, was done. If seen within 12 hours (and sometimes even after the lapse of as much as 24 hours), the devitalized and contaminated tissues, together with foreign bodies which were readily accessible, were meticulously excised. The wounds did well, particularly if supplemented with sulfonamide in adequate

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dosage by mouth. We started using sulfanilamide tablets in January, 1938, when we received our first consignment of 3000 tablets. Sulfonamide powder, however, was not used locally because it had not become available in sufficient quantity.

If radical treatment is indicated, our experience leads us to say it must be thoroughly radical. Partial excision of devitalized tissue leaves a good culture medium for bacteria to grow in, a principle which is so strongly emphasized by Trueta,[5] and others,[6] who have had extensive experience in war surgery. Furthermore, in doing the excision, it is important that longitudinal, and not transverse (except in the case of tense fascia), incision of the extremities be made so as not to cut across nerves, arteries and veins. It is also to be borne in mind that the extremity was probably in a very different position at the time the missile traversed it than the position it is found in as it lies on the operating table. This means that the tract left by the missile is found at different levels in the various muscles and all of these must be sought out if a thorough excision is to be accomplished.

In putting the emphasis on surgery being radical, however, we distinctly do not mean that it is necessarily mutilative. For instance, we saw a fresh gunshot wound in a ten-year-old boy which at first sight seemed to have completely destroyed the elbow joint. Amputation was suggested to us. Radical excision, however, of devitalized tissue followed by proper immobilization resulted in the avoidance of gross infection and the salvage of a functioning elbow joint. Similarly, badly infected elbows from gunshot wounds on more than one occasion responded to late excision through a moderately infected operative field and amputation did not become necessary.

Immobilization of the Injured Part.—Plaster encasements were used to some extent and we became very enthusiastic over our results with plaster. Our supply of plaster was unfortunately decidedly limited. Nevertheless, in almost every case some form of immobilization for rest of the part was employed. We found the Chinese had good artificers to make Thomas splints which we used considerably, often with Kirschner wire traction. There were also good carpenters who were able to make splints which conformed fairly well to the contour of the part. We frequently found, however, that our cases put up in wooden splints got manipulated by our staff entirely too much, disturbing callus formation and lighting up infection. This is one big reason why we think the plaster encasement should supersede the ordinary splint when possible and we are in accord with Trueta's[5] general principles of treatment of war wounds with plaster.

Along this line, we might mention a case of gunshot wound with compound fracture of the humerus which proved to be especially intractable. A good result was finally obtained by insertion of Steinmann pins, two in each of the two fragments, followed by incorporation of the pins in plaster after the bone ends had been freshened and approximated.

We had many gunshot wounds which caused compound fracture of the femur. We found that in most of our fractures of the shaft of the femur,

healing took place even when the position of the fragments was not perfect. What we became more concerned about was that there should not be any shortening in the length of the extremity. Kirschner wire traction of the lower fragment of the femur, while the lower extremity lay in a Thomas traction splint with the hinged knee attachment, produced good results in most of these cases.

Hemorrhage from Extremities.—One of our complications of gunshot wounds of the extremities was hemorrhage. These cases always called for balanced judgment. Often ligation of a main artery was required. The question, however, as to how other complicating factors affected the issue, usually came up. Immediate ligation sometimes puts in jeopardy the blood supply of an extremity whereas postponement for a few more days, when feasible, insures anastomoses that are more efficient in taking care of impaired circulation.

Several of our cases required ligation, two of the femoral artery and one of the ulnar artery. If seen before infection sets in, it is of course possible to ligate the bleeder in the wound. Our cases were seen late, and in all, the hemorrhage could be controlled temporarily by local compression. Our experience taught us, however, that these patients must be watched as carefully as a patient under an anesthetic, with a tourniquet already on the bed under the extremity ready to be applied. Even then, procrastination cannot be indulged in too liberally lest the patient become exsanguinated.

Again, we encountered hemorrhage in a severely infected knee in our group of 33 casualties referred to elsewhere.[3] Maggots may have been responsible for clearing away necrotic tissue from the popliteal space so rapidly that the thrombotic wall in and about the vessels was loosened, although we are aware of this happening frequently in the absence of maggots. We were faced with exhaustion which precluded early operation, hemorrhage which had produced an appreciable anemia and infection of the knee joint which could scarcely be overcome with an impaired blood supply. An attendant stayed by the bed for several days with a tourniquet, ready to apply it promptly on the first indication of hemorrhage. After building the patient up steadily for a week or so, one of our Chinese male nurses gave him some blood and we successfully amputated in the midthigh.

Amputations.—Amputations, unfortunately, were necessary in a number of cases, but the use of sulfonamides did materially lessen the number of cases in which it became necessary to perform them. In our last year we performed approximately 20 amputations out of perhaps a total of about 200 severe war wounds of the extremities which we saw. (This is a rough estimate for our records are in enemy hands and hence unavailable.)

In general, we found that where there was the slightest doubt in our mind as to whether amputation was indicated, it was best not to amputate, as sulfonamides usually turned the scales in favor of the patient in these cases. The question that caused more concern early in our experience was not so much whether to amputate, as when and where, *i.e.*, at what level.

The latter became more and more clear to us as our experience grew. One of the most important factors in determining this was the type of prosthesis which was available. Fortunately, in our early career in China (1931) we had amputated the leg of a brother of an excellent Chinese carpenter. The carpenter became greatly interested in making wooden legs and the two brothers between them made many ingenious improvements throughout the nine years he was under our observation. The appliance did not equal our modern occidental ones but it was, nevertheless, good and within the financial resources of our patients as well as being obtainable in a blockaded country. The majority of our amputations (as in the above case) were just below the knee and a bent-knee appliance was used. We do not think this is to be recommended where modern appliances are available, but it does serve to emphasize the fact that the amputation site must be adapted to the type of appliance that will be available to the patient later on, as artificial limb makers differ considerably in their ideas and products.

Many of our amputations were of the flap type. We were fortunate in being in a place where we could follow these along. The tightness of closure could be varied according to our conception of whether or not they were likely to become infected. Almost all of them were given sulfanilamide by mouth. As a matter of fact comparatively few of our clean amputations became infected. Obviously this policy of closure cannot be adopted everywhere in war surgery as widely differing circumstances alter the situation tremendously. We did, however, always immobilize and elevate our amputation stumps and we regard this as important.

Fractures of Extremities Due to War Wounds.—One of our gunshot wounds of the thigh proved especially unique. Immobilization produced healing apparently *per primam* so far as external appearances were concerned. Roentgenograms, however, showed that the missile, which was still present, had carried with it into the adductor muscles comminuted bone, representing about two inches of the middle portion of the femur together with its periosteum. Traction simply served to exaggerate the gap between the main bone fragments whereas relaxation of traction interposed soft tissue. After an interval of several months, we performed an open operation. The patient objected to a tibial graft. Accordingly, the missile and its satellite bone fragments were excised. The bone ends were then freshened and the bone fragments, which had to be broken up to extract the bullet buried within them, were put back, depositing them between the bone ends. The lower extremity and the pelvis were placed in a plaster spica for several months and firm bony union resulted without too much shortening.

Nonunion was a rather unusual complication of our fractures due to war injuries. The complication most frequently seen was persistent sinus or sinuses due to retained foreign bodies and sequestra. We found that in the type of cases of which we saw most; namely, the casualty that came to us several days after injury, it was usually best to let the fractured bones unite firmly and then go in and operate very radically. For instance,

in a case of gunshot wound of the midthigh with fracture of the femur, the bone was allowed to heal firmly. A persistent narrow sinus to the medial aspect of the thigh remained. Roentgenograms showed large sequestra posterior to the femur. The narrow sinus was slightly widened so as to admit two fingers right down to the bone, carefully avoiding injury to the neighboring vessels. Then a long longitudinal incision was made posterolaterally, exposing the sequestra widely and removing them completely under direct vision. This incision was decidedly radical and was planned so that healing would start from the depths of the wound and take place gradually as packing was extruded. This long wound was packed wide open with vaselined gauze and a wick of vaselined gauze was put into the widened medial opening, following which the part was immobilized. With such treatment we found that most of our extremity wounds healed with no further complication.

Gunshot Wounds of the Pelvis.—Gunshot wounds of the pelvis presented a more serious problem. The osteomyelitis that developed here was not so easily treated as that of the extremities. As we look back at these cases, we feel that probably our failure lay in not opening up widely, cleaning away sequestra fully, and packing them thoroughly enough. In any case, osteomyelitis of the pelvis presents a serious problem, especially in view of the contiguity of contamination from body excretions and the type of bone involved. In one of our gunshot wounds, the bony sequestra from the pelvis were carried through the bladder into the abdomen and deposited there. Primary suture of the bladder was successful in restoring normal bladder function, but the bony sequestra were not discovered until some weeks later when the omentum, which had wrapped itself around them, delivered them at the wound of exit, where it was possible to extract them by a very minor procedure.

Gunshot Wounds of the Abdomen.—If there is indication of a penetrating wound of the abdomen, our experience taught us it is really advisable to explore the abdomen promptly, providing one has the time and place available to do it. Often seemingly innocuous wounds of the liver result in fatal hemorrhage which is appreciated too late, while perforations of the intestine must be closed early to avoid continuous peritoneal contamination. Our results in this category were frankly bad. We saw a case of fatal hemorrhage from a gunshot wound of the liver which we believe could have been arrested if we had not adopted the policy of watchful waiting. Our perforated intestine cases, on the other hand, we felt did not do so well partly because we got them too late. Furthermore, we are inclined to feel that in some we wasted too much time in doing a two-layer closure of the bowel. In view of the serious condition of these patients, we are inclined to recommend closure with a single layer of carefully approximated silk or cotton suture.

In one case we failed to find the wound of exit from the stomach, figuring, at the time, that the bullet, which we found lying free in the abdomen, had merely penetrated the anterior wall of the stomach through which it had subsequently been extruded, and had not penetrated through both walls

of the stomach. The subsequent clinical course leads us to think that a more careful search by exposure of the posterior wall of the cardiac end of the stomach would doubtless have disclosed a wound of exit. Incidentally, the old rule-of-thumb we found was a good one; namely, that gunshot wounds of the gastro-intestinal tract occur in even numbers; *i.e.*, one of entrance and one of exit.

Chest Wounds.—As to exploration of chest wounds, the cases we saw in which this might have been done to advantage, were seen under conditions where our operating facilities did not warrant it, and this, we think, is an important matter. A chest exploration cannot be undertaken without an expert anesthetist. On the other hand, the sucking wound of the chest, which really may represent a fairly serious situation, we found we could take care of with the simplest of facilities.

Chinese soldiers in civilian clothes had made a raid on the city where we were stationed. The Japanese, in an endeavor to round them up, issued restrictions against any one giving lodging to wounded Chinese. This meant we could not let these casualties come under our roof without incurring the displeasure of the Japanese whose protection we then enjoyed. Well do I remember under these circumstances operating in our front court-yard under the open sky upon a Chinese soldier with one of these sucking wounds from a bayonet stab. We simply injected a little local anesthesia, put in a few silk sutures, strapped the chest tightly with adhesive, and sent the man on his way. He reported later to the clinic as directed, and made a good recovery.

Many of our gunshot wounds of the chest responded to simple rest in bed, and sulfonamide by mouth. Unless there was obvious hemorrhage or infection, we felt that it was best to leave bullets which had lodged in the lungs or mediastinum strictly alone.

In cases of infection, it was usually possible to deal with a well-localized empyema by simple rib resection and drainage. In cases of hemothorax, frequent aspiration should be done as long as blood accumulates so as to remove a potent culture medium. When seen early, we found that auto-transfusion of the aspirated blood was decidedly beneficial, but we would emphasize that there is grave danger of transfusing infected blood after 24 hours have elapsed, and there ought always be a bacteriologic check on it. Sometimes there is no way of stopping hemorrhage aside from exploration and ligation of the bleeder. This should not be delayed too long, particularly when a closure of the chest wall has broken down under the pressure of increasing hemothorax.

Head Wounds.—Ordinary bullet wounds of the head, we usually were able to leave alone without unfortunate results. Roentgenograms ordinarily would show the bullet safely couched in some area of the brain where non-intervention would probably cause less damage than its removal. We encountered one case of middle meningeal artery hemorrhage which we might have saved if we had diagnosed it earlier. The patient had a bullet fired

quite close to his temple and the general contusion of the brain was possibly as great a factor in his rapid demise as the actual hemorrhage.

Another of our patients had a severe injury of the head of a rather different type. Banditry was rife in the district surrounding our hospital after the Japanese had taken over the city. Early one morning a bandit came to a farmhouse, where all the members of the household submitted to his demands except the farmer's wife. She was of low mentality and resisted. The bandit picked up the meat cleaver and proceeded to hack away at the vault of her cranium. When she arrived at our hospital, a mass of hair, bones, gray matter and skin presented itself over the left frontoparietal region. Persistent cleansing with soap and water and physiologic saline, cutting and shaving of hair, excision of devitalized skin, removal of bone fragments which had become detached from the pericranium, and cutting away of contaminated and apparently superfluous gray matter, permitted of closure of the scalp. Healing *per primam* followed, and her relatives and friends all insisted that she was greatly improved mentally after our operation!

Sulfonamide Treatment for Erysipelas and Gas Gangrene.—Excessive handling, together with improper original toilet because of being seen too late, seemed responsible for the production of erysipelas in some of our burn cases. One of these came down with a fulminating attack of erysipelas which progressed promptly into coma. Five hundred cubic centimeters of a solution of one-half per cent sulfanilamide in physiologic saline was administered intravenously, followed by 200 cc. every four to six hours, with most gratifying results.

Similar administration of sulfanilamide was also resorted to in our gas gangrene cases.[3] Immediate amputation had been disappointing in our earlier cases. In our later cases, amputation was postponed until after the acute phase had well subsided. In fact, it did not always prove necessary. Despite the fact that we did not have antitoxic serum for gas gangrene available, we succeeded in carrying our last four cases through on sulfanilamide therapy, the first day intravenously and on subsequent days orally, to a successful issue, although on the first two or three days they were very toxic. These cases received no local treatment aside from establishment of drainage in the simplest manner, changes of dressings and immobilization, as indicated. An unfortunate cross-infection into a fresh amputation in the hospital convinced us of the high infectivity of the discharges from these wounds.

Treatment of Tetanus.—Tetanus was encountered particularly in badly contaminated cases which did not receive proper early treatment. One case stands out in our mind, of a man who had been reduced by the circumstances of war to scavenging in order to eke out a living for his wife and himself far away from their original home, which the Japanese had burned down at the same time that they had brutally slain their children. Unwittingly he picked up a hand grenade and tried to pry it open. The greater part of his hand was blown off, and he received no treatment until he came to us

some days later with a necrosing wound. We prescribed hot magnesium sulphate soaks and sodium hypochlorite wet dressings, also giving a prophylactic injection of 3000 international units of tetanus antitoxin. He shortly developed tetanus from which he did not recover. As we look back on this case, amputation in the midforearm might have saved his life even after he developed the first symptoms of tetanus.

Another case of tetanus developed in a Chinese farmer whom, together with all the young men of his village (about 40 in all), the Japanese had captured and bound in a kneeling posture, lined up with his fellow-villagers in a dry river bed. Forty Japanese soldiers took their position along the bank and each one was ordered to fire one shot at his respective target. The soldiers were then told to investigate how successful they had been in killing their targets. Those who had been unsuccessful, picked up large stones from the river bed and bashed in the skulls of their victims. Our patient had a very copious hemorrhage from his right femoral vessels and was thought to be dead. Accordingly he was left. After about two hours, he revived sufficiently to drag himself to his home nearby where he remained until he started to develop symptoms of tetanus. He was then brought to us and we found a suppurating pocketed wound of the thigh. We débrided the wound; *i.e.*, established thorough dependent drainage, removing all foreign bodies and loose necrotic tissue. About 40,000 international units of antitetanic serum were given intravenously. He was also given an intraspinal injection of 25 per cent magnesium sulphate (7 cc.) according to the technic outlined by Beckman.[7] Thorough relaxation was produced to such an extent that respiratory arrest ensued. Calcium chloride intravenously seemed to have little effect in counteracting this, despite Beckman's claim for this as an antidote. Artificial respiration was carried out on him for 16 hours after which he started breathing spontaneously. He experienced no further convulsions and made a full recovery. Trueta's[5] views on the beneficial effects of immobilization resulting from muscular relaxation in this condition are interesting in the light of this experience. We feel more strongly than ever that elimination of the nidus of infection, even after the development of clinical tetanus, is definitely indicated, although we are aware of disagreement on this subject.[5]

Methods of Anesthesia.—As regards methods of anesthesia, we found that the simplest served us best under the circumstances. Local anesthesia with novocain was utilized in many of our minor casualties. Open drop-ether was used extensively. Intravenous evipal was also used in a few instances. Spinal anesthesia and brachial block were employed a great deal, but mostly for cases upon which we were operating a matter of days after injury, where the reaction was favorable. We feel that brachial block and spinal anesthesia in particular are best reserved for cases which are not suffering from shock immediately following war trauma.

Utilization of Roentgenography.—As to the use of roentgenography, earlier in the war we had the advantage of obtaining good films, but during the last

year or so, we were working in a place where the Chinese guerillas blew up the electric power plant (December, 1939). Subsequent to this, our electric power was only sufficient for the use of the fluoroscope, and that at only certain times of the day. We got into the habit of tracing the outline of a fluoroscopic shadow on transparent paper superimposed on the screen. We hung up these tracings in the operating room and found them very useful guides as we operated, for usually the pieces of metal or bony sequestra showed up in sharp relief in relation to the intact bone and soft tissues.

Special Surgical Problems.—War surgery always is fascinating because each case presents a new problem or combination of problems. Not only is there a multiplicity of missiles, but of the anatomic parts in which they locate and of the directions they take in the human body in its varied contortions. This makes an infinite number of combinations possible. Nevertheless, it seems to be the case everywhere, and our experience was no exception, that wounds of the extremities are decidedly in the majority. Doubtless many of the wounds of other regions are not so generally amenable to treatment and prove fatal even before seen by the surgeon. Then too, it must be realized that the extremities present a large surface area for encountering missiles out of all proportion to their comparative weight.

One of our unique problems was a gunshot wound of the perineum in which the bullet lodged in the lumen of the bulbous and lower membranous urethra. Owing to the contamination of the urethra together with the scorching of the surrounding tissues, it became necessary to open the perineum widely, making the urethra continuous with the rectum as a cloaca. This entire area was permitted to epithelialize. Following a suprapubic drainage, the adjacent rectal mucosa was undermined and brought forward in two lateral portions continuous anteriorly with the urethral mucous membrane. These were sutured together in the midline posteriorly to reconstruct an over-sized bulbous urethra, thereby allowing for subsequent scar-tissue contraction. Then long muscle strips from the two glutei maximi were turned in across the midline to form a new perineal body and anterior anal sphincter. This in turn was covered by redundant upper anterior rectal wall mucous membrane which was freed and brought down so as to suture it in place without tension. A good result was obtained.

Another patient came to us with a fecal fistula of the lower ileum near the cecum, complicated by osteomyelitis of the ilium. This was acquired ten years previously from a gunshot wound in one of China's civil wars. Here, again, we were confronted with some interesting multiple-stage operating. First, the lower ileum proximal to the fistula was anastomosed by side-to-side anastomosis to the transverse colon by aseptic technic to partially divert the fecal current. Then the fistulous area was cleaned-up superficially down to the actual perforation. The fistula was given a chance to heal spontaneously but refused to do so. Finally, the peritoneal cavity was opened up in the region of the fistula and the nearest well-nourished segments of intestine on either side of the fistula were anastomosed

by end-to-end anastomosis after cutting away granulation and redundant tissue. The fistula then healed. The osteomyelitis of the ilium was subsequently attacked and sequestra removed. When last seen, he still had a granulating wound which showed every sign of healing subsequently.

SUMMARY

Our experiences in war surgery in China have been recounted, particularly as related to: (1) Preoperative preparation of the patient; (2) excision of war wounds; (3) immobilization of the injured part; (4) control of hemorrhage; (5) amputations; (6) war wounds of specific regions—extremities, pelvis, abdomen, chest and head; (7) sulfonamides in erysipelas and gas gangrene; (8) treatment of tetanus; (9) methods of anesthesia; (10) utilization of roentgenography; and (11) special surgical problems.

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BRIEF COMMUNICATIONS

MACRODACTYLY*

CASE REPORT

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FOR PURPOSES of interest and record, unusual examples of congenital anomalies are from time to time reported. The following case of macrodactyly, or partial gigantism, affected only one digit. No discernible cause could be found. The child, otherwise, is of normal mental and physical development. There is no family history that would tend to explain its occurrence.

Case Report.—M. M., age three, female, was admitted to the First Surgical Division of St. Vincent's Hospital, October 10, 1931. The chief complaint was an enlargement of the right middle finger. The mother stated that at the time of the child's birth, the middle finger of the right hand was much larger and longer than the other fingers of the same hand. She stated that since the time of birth the right middle finger had grown rapidly. This growth was far out of proportion to the child's age and to the other fingers of both hands. Careful questioning elicited no history of any familial tendency or influence to overgrowth. The general past history is irrelevant.

Physical examination showed a well-developed and well-nourished white child, three years of age. She showed no evidence of malformation other than the middle finger of the right hand. The findings, on general physical examination, corresponded with those of any normal child of the same age. Routine laboratory findings were reported as being within normal limits.

Local Condition.—The middle finger of the right hand, together with the nail, shows a diffuse, symmetrical hypertrophy of about five times its normal size. This is judged by the corresponding finger of the other hand. There is an abnormal increase of motion of the distal phalanx, which can be easily hyperextended, without pain. There is also an extension of the enlargement running into the palm of the hand superiorly to the thenar eminence. This swelling appears to be the flexor sheath and tendons of the middle finger. The remainder of the digits of both upper and lower extremities are normal.

Roentgenologic Examination.—Dr. W. W. Maver: The right third digit showed abnormal development of the bone structures, without changes in their contour or density other than a broadening of the distal phalanx. *Roentgenologic Diagnosis:* Gigantism.

It was planned to amputate the finger and remove its corresponding metacarpal bone, but the wishes of the mother were acceded to, and a plastic operation was undertaken. The distal phalanx was amputated in order to lessen the length of the finger. Wedge-shaped excisions of soft tissue were performed on either side of the middle and proximal phalanges in order to lessen its circumference. Primary union occurred, but, as was to be expected, the cosmetic and functional result was poor.

The patient was readmitted to the hospital June 23, 1933. Examination showed that the right middle finger, which previously had an amputation of the distal phalanx, was

* Submitted for publication October 28, 1943.

enlarged to about six times its normal size. This enlargement extended on to the palmar surface of the hand. It involved the tendons and sheath of the right middle finger. An amputation of the finger with its corresponding metacarpal bone was performed.

Operative Procedure.—A racquet incision was made about the base of the right middle finger. This was extended on to the palm of the hand superiorly to the thenar eminence. Skin flaps were dissected away from the tendon sheath and soft tissues. The sheath and tendons were divided at the transverse annular ligament of the wrist joint and drawn inferiorly. The attachments of the adductor pollicis transversus muscle were separated from the volar surface of the middle metacarpal bone. The lumbrical and interosseous muscles were freed. The volar ligaments from the middle metacarpal

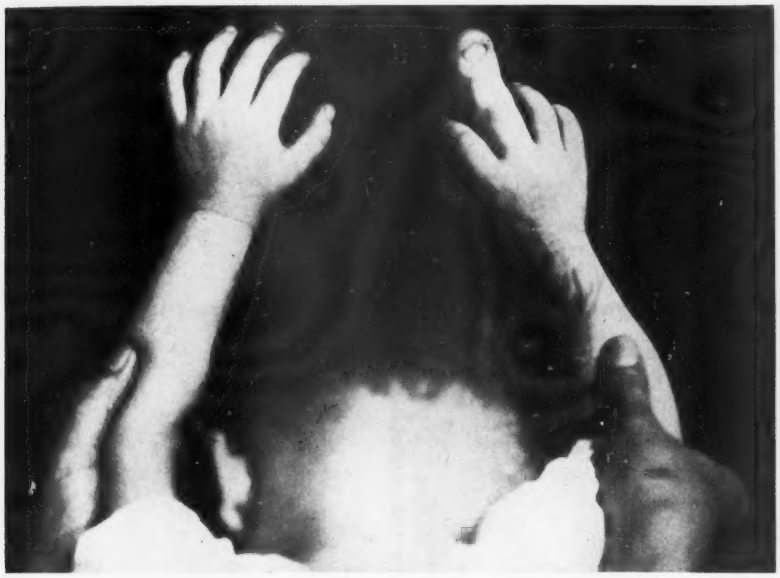

FIG. 1.—Photograph of condition preoperatively.

bone to the carpus were divided. A one-inch incision was made on the dorsum of the hand over the proximal end of the middle metacarpal bone, and its dorsal attachments to the carpus were severed. The finger, with the corresponding metacarpal bone, flexor tendons and sheath, was then removed. Bleeding points were clamped and ligated. A periosteal suture taken at the distal ends of the second and fourth metacarpal bones, closed the space between them. The skin was united with interrupted silk sutures. A rubber tissue drain was placed in the space between the index and ring fingers. The drain was removed in two days. Primary union occurred.

Pathologic Report.—Dr. A. Fraser: Sections show signs of abnormal rapidity of growth, both in periosteal and in cartilage replacement bone. The soft tissues show proportional increase in size. Otherwise, the tissues of the finger are normal.

Postoperative Course and Follow-up.—The patient had normal function of all fingers except for a temporary limitation of adduction of the thumb. It is assumed that this was due to division of the adductor muscle at its origin on the middle metacarpal bone. Since that time, all motion has returned to a better-functioning and better-appearing hand. The patient, who is right-handed, is now able to use her right hand in writing, eating, playing, *etc.* She is evidently unmindful of the change brought about.

FIG. 2

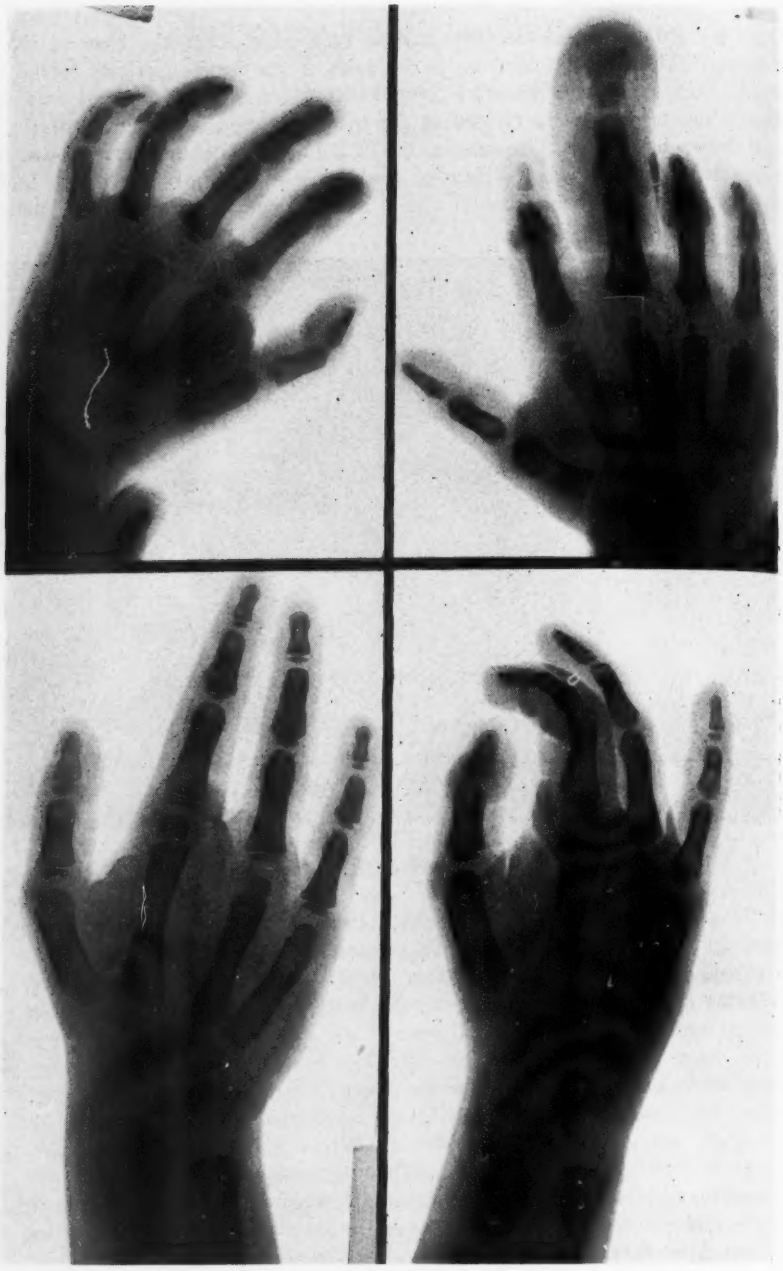

FIG. 3

FIG. 2.—Preoperative roentgenogram of both hands for comparative study.
FIG. 3.—Roentgenologic study of postoperative result.

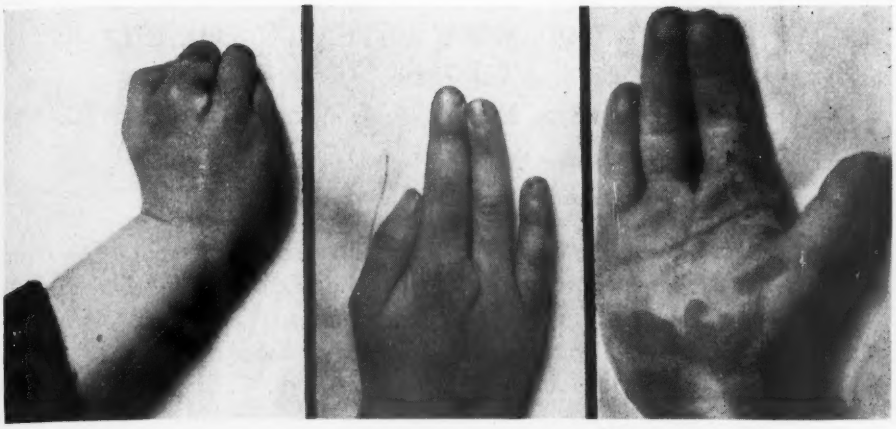

FIG. 4.—Photographs of end-result.

SUMMARY

Macrodactyly, a congenital anomaly of the hand, affecting only one (right middle) finger is reported. A method of handling this condition so as to give a better-functioning hand, with an improved cosmetic result, is described.

EPIDERMOID (SQUAMOUS EPITHELIAL) BONE CYST OF PHALANX*

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Tumors involving the bones of the hand are quite rare. Coley and Higginbotham[1] found in the material from the Memorial Hospital and the Ruptured and Crippled, in New York, among 1211 bone tumors twenty involving the bones of the hand. They reviewed the American and foreign literature up to 1939 and found only 136 such cases. The following entities are mentioned—osteogenic sarcoma, endothelioma (Ewing's tumor), giant cell tumor, chondroma, simple bone cyst and metastatic carcinoma.

A new type of single neoplastic bone lesion of the hand was first described by Sonntag,[2] in 1923. Although it is mentioned in several textbooks,[3] only ten proven cases of epidermoid cyst of the phalanx have, to our knowledge, been reported. This condition has to be considered in the differential diagnosis of every case in which the radiologic examination shows central destructive bone lesion situated in a terminal phalanx of the hand. To discuss the pertinent clinical and pathologic features is the purpose of the report of our case.

Case Report.—A 50-year-old, white, railroad employee injured the tip of his left middle finger one year ago while applying the brakes on a railroad car. The finger was very sore for some time; the nail was discolored, but did not come off. He did not consult a physician at that time. The soreness of the finger disappeared although this finger remained somewhat more sensitive than the others. About six months later he injured the same finger again, by pinching it in a drop-door. The finger became more sensitive since the second accident, and was periodically red and swollen, especially so three weeks before his admission to the hospital. Physical examination showed tenderness, redness and moderate swelling of the soft tissues around the distal phalanx of the left middle finger. Pressure was quite painful. Motion was normal. There was no fever or other systemic symptoms. The blood count was normal.

Radiologic Examination.—Dr. J. Walton: This revealed soft tissue swelling in the region of the distal phalanx of the left middle finger. The middle third of the distal phalanx shows a fairly well circumscribed, circular destructive process—revealing an area of translucency which by expansion has broken through the cortex laterally, medially and dorsally but without destruction of the tip or the proximal end of the phalanx (Fig. 1).

Operation.—Under pentothal sodium anesthesia, the finger nail of the left middle finger was removed. A longitudinal incision was then made and the dorsal surface of the bone opened. A cystic lining presented itself, which was opened. The cyst was filled with sebaceous-like material. The whole cyst was easily peeled of its bony bed. The bony cavity was then cauterized with electric cautery. The further treatment was a modified Orr procedure. Vaselined gauze was packed into the cavity and sulfanilamide dusted over the wound, and a plaster encasement applied to the finger. The postoperative course was uneventful.

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Pathologic Report.—Specimen consists of an opened cyst wall measuring on reconstruction about 1 x 0.8 x 0.6 cm. Surface is smooth and glistening white. A good amount of the contents of the cyst, consisting of amorphous, yellowish sebaceous-like material has also been received.

Microscopic Examination.—The wall of the cyst is made up by stratified squamous cell epithelium. It consists of a well developed stratum spinosum and a stratum granulosum which is formed by one to two cell layers and a thick horny layer. The latter is obviously forming the dense keratinized contents of the cyst. In several areas a thin layer of fairly vascular connective tissue is found at the outside of the cyst wall (Fig. 2).

Since in this case, as well as in all other described cases, no dermal structures (sebaceous glands, hair follicles) were found, the classification of the lesion as epidermoid cyst seems justified.

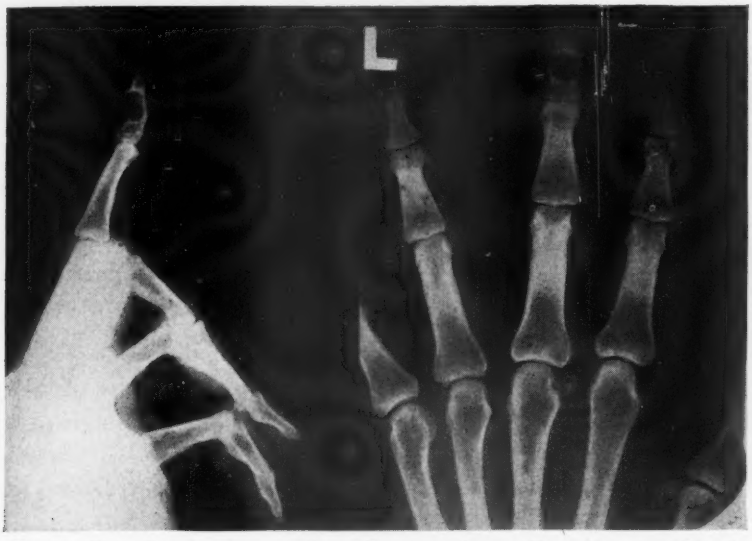

FIG. 1.—Lateral and anteroposterior radiograms of an epidermoid cyst within the terminal phalanx of the left middle finger.

Postoperative Course.—Swelling, tenderness and pain have completely disappeared. The fingernail has grown to the end of the finger. The distal phalanx is somewhat shortened. Radiologic examination six months after operation shows the circular translucent area previously reported partially obliterated. The distal portion of the phalanx is now almost in contact with the proximal half and slightly angulated forward due to almost complete obliteration of the pathologic area. There is no apparent union or filling-in of bone in the area (Fig. 3).

COMMENT: Epidermoid cyst of the phalanx appears to be a distinct clinical and pathologic entity, as can be seen from the review of the cases in Table I and our own case.

The following is a summary of the most important features: Sex: Eight patients were male; three were females. Age: Two patients were adolescents. The age of the others was between 29 and 50 years.

History: All patients with exception of Cases 5 and 7 gave a definite history of previous injury to the respective finger. The sustained injury was varying

in degree. In several instances it was described as quite serious; in others as slight. The patients with negative histories may also have sustained slight injuries to which they did not pay any attention. The time between first injury and appearance of symptoms varied between 1 and 35 years. In several cases subsequent injury caused, apparently, rupture of the bone tumor with consecutive expansion into the soft tissue.

Symptoms: All patients noticed swelling of the respective fingers. Nine out of 11 experienced pain and tenderness of the finger, especially if the finger was accidentally struck. Five noticed a reddening of the swollen part. No fever or other systemic symptoms were present.

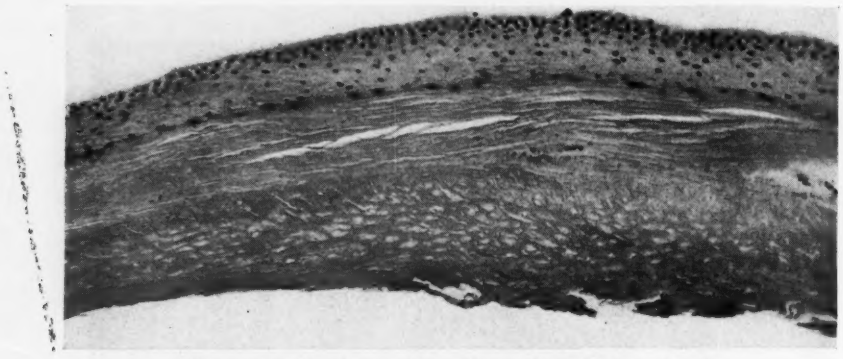

FIG. 2.—Section from epidermoid cyst from phalanx. (× 50)

Clinical Findings: In ten cases swelling was found at the distal end of one finger; only in Case 1, in which the distal phalanx had been previously amputated, the swelling was found in the end of the stump. There was pain on pressure in the majority of cases. The motion of the finger was not impeded.

Radiologic Examination: The radiograms showed a distinct area of destruction in the terminal phalanx. This translucent area is homogenous, fairly well circumscribed and more or less circular. In one case the cystic area showed irregular vacuolation, in one other case two confluent cysts could be recognized. The lesion is in most cases centrally located. Occasionally it was found nearer to one side of the bone (eccentric). The cortex of the phalanx is frequently expanded. A thin shell of bone may remain or this shell may be completely destroyed in one or more areas, thus leading to pathologic fracture. The lesion is in the majority of cases seen in the distal portion of the terminal phalanx. It occurs, however, also in the middle third or proximal part. It may replace the phalanx entirely. There is no significant periosteal reaction present.

Differential Diagnosis: Since in all cases only a single lesion has been observed, all diseases which lead to multiple bone involvement are easily excluded; *e.g.*, ostitis fibrosa generalisata, multiple myeloma and metastatic carcinoma. The most frequent lesion to cause central bone destruction in a phalanx is enchondroma (Geschickter and Copeland[12] and Jaffe and Lichten-

REPORTS OF EPIDERMOID BONE CYSTS OF PHALANX

No.	Author	Age	Sex	History and Clinical Findings	Radiogram	Treatment	Histopathology
1	Sonntag[2] (1923)	44	♀	Injured the left hand in a machine, crushing the terminal phalanx and the distal part of the middle	Transparency of the distal half of	Amputation of middle	Epithelial cyst.

REPORTS OF EPIDERMOID BONE CYSTS OF PHALANX

No.	Author	Age	Sex	History and Clinical Findings	Radiogram	Treatment	Histopathology
1	Sonntag[2] (1923)	44	♀	Injured the left hand in a machine, crushing the terminal phalanx and the distal part of the middle phalanx of her 4th finger, which was amputated 24 years later. Development of swelling in the stump with pain and increased tenderness upon pressure.	Transparency of the distal half of the remaining middle phalanx.	Amputation of middle phalanx.	Epithelial cyst.
2	Burrows[4] (1926)	47	♂	At age of 11 ran a piece of wire deeply into his left thumb. 35 years later end of this thumb became swollen. 8 months later a piece of metal fell on this same thumb. Thumb became more swollen, tender and painful.	Irregularly vacuolated cyst occupying nearly completely the terminal phalanx.	Amputation of distal phalanx.	Contents of the ruptured cyst wall, consisting of white material resembling hydrous wool fat, were found under the skin. The bone was occupied by a single ramifying cyst. The wall of the cyst was formed by fibrous tissue lined by stratified epithelium.
3	Friedländer[5] (1930)	13	♂	Injury to left index finger 1 year ago. There was swelling of the finger but no pain.	Expanding cystic lesion with destruction of distal two-thirds of terminal phalanx.	Amputation of distal phalanx.	Smooth cyst filled by sebaceous-like material invested by hornifying epithelium; on one area intermingling granulation tissue containing foreign body giant cells.
4	Hammann[6] (1930)	31	♂	Injury to right index finger by hammer blow 16 years ago. Swelling and reddening of this finger and pain whenever finger was struck.	Small, somewhat eccentric, transparent mass destroying the bone in the radial and dorsal side under the nail bed.	Extirpation of cyst. Complete cure.	Cyst lined by stratified epithelium. Contents partially encrusted by calcium.
5	Harris[7] (1930)	Adult	♂	Golf champion. Severe pain and disability of the left thumb 5 years ago. Tenderness persisted and became recently greater and accompanied by swelling. No definite trauma at any time.	Destructive cystic lesion of distal half of terminal phalanx.	Excision of cyst.	Fibrous cyst wall lined by squamous epithelium.
6	Behrens[8] (1931)	29	♂	Hand grenade wound in right 5th digit 11 years ago, complete healing; 6 years ago same finger hit by hammer blow. Since then finger became painful, swollen and reddened.	None reported.	Amputation of terminal phalanx.	Squamous epithelial cyst in phalanx underneath the nail bed.
7	Curtis & Owen[9] (1933)	29	♂	Swelling and reddening of distal phalanx left third finger with throbbing pain 8 years ago. 4 years later a cyst was excised, with little relief. Distal portion of finger twice of normal size, tender to the touch. No history of definite trauma.	Two confluent cystic lesions destroying all but the base of the distal phalanx.	Excision with recurrence. Second excision resulted in permanent cure.	Two cysts found in the partially destroyed terminal phalanx. Cyst wall composed of fibrous tissue lined by squamous epithelium. The cysts contained sebaceous-like material.
8	Bissell & Brunschwig[10] (1937)	Girl	♀	7 years ago injury to finger. Swelling of terminal phalanx.	Rounded well circumscribed, expanding cystic lesion in the proximal half of terminal phalanx.	Excision of cyst. Complete filling-in of defect seen in X-ray.	Squamous epithelial lining surrounding laminated keratin.
9	Bissell & Brunschwig[10] (1937)	41	♂	Severe injury to left index finger 10 years ago. Swelling of the terminal portion of the finger, with slight tenderness on pressure.	Expanding cystic lesion replacing all but the base of the terminal phalanx.	Excision of cyst.	Cyst lined by stratified epithelium containing sebaceous-like material.
10	Yachnin & Summerill[11] (1941)	39	♀	Injury to terminal phalanx of right fourth finger two years previously. Swelling but no redness of the end of the finger for several months, with moderate pain for the last three weeks. 5 months after excision of cyst gradual increase in tenderness but no swelling.	Circular area of destruction in distal part of terminal phalanx, with extension into the periosteum on the radial side.	Excision of cyst. Five months later amputation of distal half of terminal phalanx.	Cyst wall composed of stratified squamous epithelium surrounding a nest of keratin débris.

stein.[13]) Trauma is often recalled in connection with the appearance of this tumor, but not a trauma dating back such a long time as frequently observed in epidermoid cyst. Swelling and pain are mostly moderate. Radiograms may show a very similar appearance to that found in epidermoid cyst; however, trabeculation of the cystic space with small areas of increased density are frequently seen.

Simple bone cysts are very rare in the phalanx. Jaffe and Lichtenstein,[14] in a recent publication, doubt whether they ever occur in the bones of the hand or feet, although single instances in this location have been reported. They occur nearly always before the age of 20. They usually cause no symptoms before fracture occurs. The radiogram shows, as a rule, no, or only little, trabeculation in the cystic area. The third cystic bone lesion

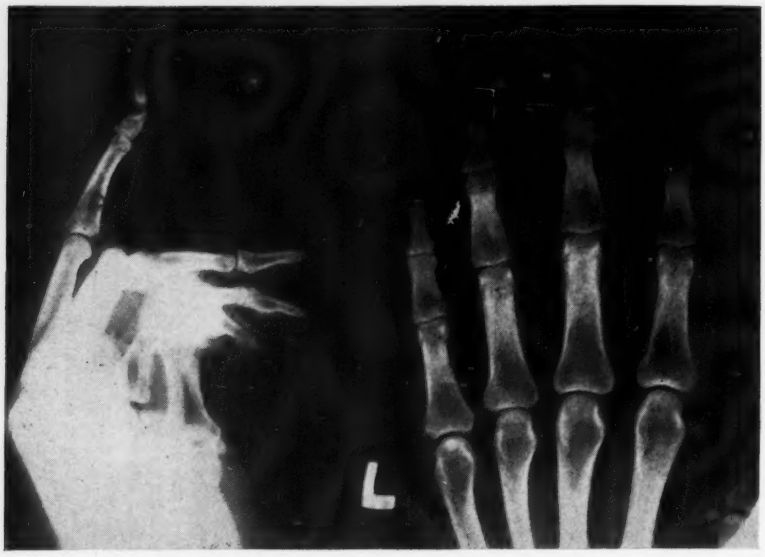

FIG. 3.—Lateral and anteroposterior radiograms six months after excision of an epidermoid cyst.

—giant cell tumor—is also very rare in the phalanx of the hand, somewhat more frequent in the metacarpal bones. It occurs mostly in the 3rd decade of life. Trauma is usually recalled. The tumor develops fairly rapidly, causing distinct discomfort. The history is usually fairly short. The radiogram shows the area of bone destruction traversed by fine trabecules.

Osteogenic sarcoma and endothelioma (Ewing's tumor) are extremely rare in the phalanges of the hand. Their radiologic appearance varies so markedly from the central cystic lesion of epidermoid cyst without periosteal reaction that the differentiation should not offer much difficulty.

Inflammatory lesions rarely produce a picture that imitates the epidermoid cyst of the phalanx. Brodie's abscess, a form of chronic osteomyelitis, occurs usually in the tibia, showing quite distinct thickening of the bone around the cystic area. A bone gumma is rarely found in a phalanx. Periosteal reaction

is usually quite prominent. If any doubt exists, history and Wassermann reaction will be of great help.

In the differential diagnosis endochondroma has, therefore, to be considered primarily. Simple bone cyst and giant cell tumor have also to be taken into consideration. If the decision cannot be made on the basis of radiographic and clinical findings, the diagnosis can be made at operation without difficulty, since the appearance of the white, glistening cyst wall filled with sebaceous-like material is absolutely characteristic.

Therapeutic Procedure: In four cases the phalanx containing the cyst was amputated. In six cases the cyst was excised. In two of these cases recurrence occurred after removal. In one case the second excision led to complete cure; in the other case the distal part of the phalanx was removed, with good result. It seems that our procedure to open the bone, remove the cyst, and then to cauterize the bony cavity carefully is of definite advantage. It preserves the finger and prevents possible recurrence of the tumor.

Etiology: The etiology of this tumor has been recently discussed by Yachnin and Summerill.[11] The cysts resemble the implantation cysts that have been found in the soft tissues of the finger and hand, especially in tailors and seamstresses. Two different theories concerning their etiology are found in the literature: (1) Congenital maldevelopment, with embryonal misplacement of epithelial cells; or (2) traumatic implantation of epithelial cells into deeper structures. Experimental work supports this latter view. It is quite probable that the epidermoid cysts in bone are also caused by implantation of epithelial cells. In some cases (Behrens[8]) the continuation of epithelial cells from the injured skin into the bone could be seen microscopically. The implantation of epithelial cells into the bone may occur through a very small fracture or by transmission along the vascular channels (Yachnin and Summerill[11]).

SUMMARY

A case of epidermoid cyst within a phalanx is reported. The clinical, radiologic and pathologic findings of the cases hitherto described in the literature are summarized, and the differential diagnosis of this tumor of the bone is discussed. Treatment by excision with following electric cauterization is recommended.

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PRESACRAL DERMOID*

Case Report

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Camp Forrest, Tenn.

As a result of the physical examinations incident to the mobilization of large numbers of individuals for war and industry, there has been a renewed interest in the various congenital defects to which we find ourselves heir. Of these, various involvements of the sacral region are frequently found. Simple pilonidal sinuses have been observed in two to five per cent of young adult males,[6] but their incidence is much lower in females. However, there is a congenital anomaly of the sacral region which has been described as occurring only in females. This is the presacral dermoid.

The incidence of these tumors is quite rare. Whittaker and Pemberton[7] were able to find nine cases at the Mayo Clinic. They state an incidence of ventral tumors of all types of one in 40,000 registrations, and from their statistics Manheim, Druckerman, and Peskin[3] computed only one dermoid cyst in 97,000 registrations. Lahey and Eckerson[2] report three cases from the records of the Lahey Clinic. All cases reported were in females. Manheim, Druckerman, and Peskin report one case from Mt. Sinai Hospital, which was the only known case at that institution.

The derivation of this tumor, as that of the other tumors, which involve the complex embryonal process of the caudal extremity, is obscure. The dermoid tumor is of necessity ectodermal in origin, and those ventral to the sacrum may arise possibly from either of three structures: (1) Proctodeal membrane; (2) postanal gut; and (3) vestiges of the neurenteric canal.

(1) *The proctodeal membrane* is usually the origin of tumors of the pelvic connective tissue or nodules of the penis or scrotum.

(2) *Postanal Gut.*—This is the terminal portion of the hind gut which is "pinched off" following the union of the protodeum and the hind gut at a slightly higher level. This portion usually atrophies but may be the origin of classical cystic tumors between the coccyx and the rectum described by Middledorpf,[4] and later bearing his name. This tumor contains an isolated, convoluted, portion of intestine surrounded by fat.

(3) *Vestiges of the Neurenteric Canal.*—It is from this source that it would seem most likely that a simple presacral dermoid would develop. It is generally agreed that they arise from a portion of ectoderm that is separated during a faulty coalescence or invagination of a portion that failed to atrophy.

The simple dermoid, as found in this region as well as in other parts of the body, represents one of the simpler forms of cystic tumors, the wall of which is composed of the epidermis, derma and their structures. They contain

* Case studied while attached to Station Hospital, Fort Oglethorpe, Ga. Submitted for publication September 4, 1943.

a thick, often foul smelling sebaceous material and frequently hair. They may be single or multilocular.

Occurring in the coccygeal and presacral regions are the related and more complex neoplasms from which the simple dermoid must be differentiated. These include the chordomata, whose histologic appearance is that of the primitive notochord, and teratomata comprising the three embryonic germ layers. The latter is a large group in which most writers place poorly defined and differentiated tumors comprising two or more types of tissue. These

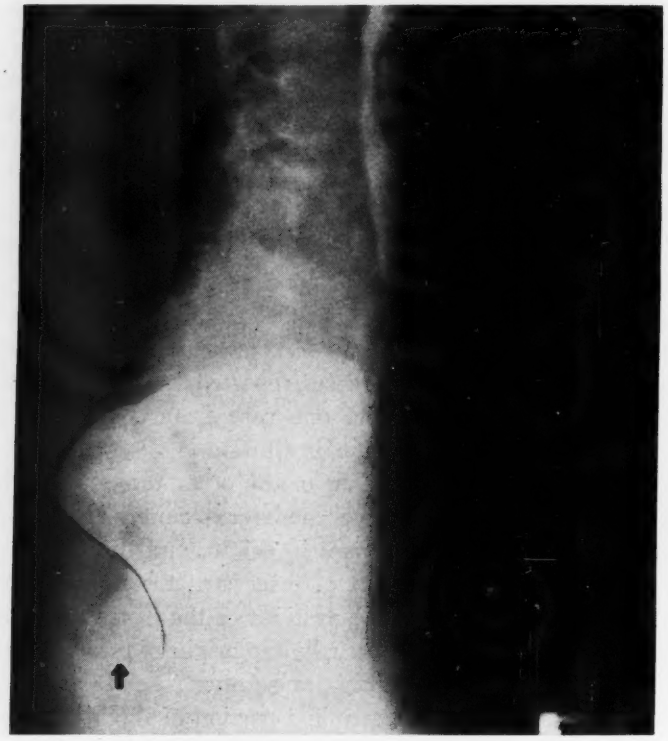

FIG. 1.—Lateral roentgenograms following barium enema. Anterior border of the tumor has been outlined on the film. (All photographs are by the Army Signal Corps.)

tumors are most commonly seen in infants. Of these, one-third are born dead, and 90 per cent of the remainder die during the first few days of life.[1] Very rarely we find other types of tumors arising from the bone, cartilage or other connective tissues. Walker and Pemberton[7] report a fibrosarcoma, a chondromyxosarcoma, and a fibroma in their series.

Case Report.—No. 81736: A. H., white, female, age 21, a W. A. C. auxiliary, was admitted to the Station Hospital, Fort Oglethorpe, Ga., April 23, 1943. She had had no complaint but was referred because of a mass found in the pelvis at routine examination. She had had no operations or serious illnesses. She had never suffered from constipation.

Physical Examination.—The patient was a tall, thin individual. Weight 120 pounds. Height five feet eight inches. Her general examination revealed no abnormality except

that found in the pelvis. There was a slight vaginal discharge. The cervix was normal to palpation. The uterus was normal size and position. A speculum could not be inserted due to a mass the size of a small grapefruit, which bulged into the posterior vagina. By rectal examination it was determined that this mass lay posterior to that structure. The mass itself was not tender and was cystic, having a soft mushy consistence. There were no abnormalities of the coccygeal or anal region.

By proctoscopic examination the mucosa overlaying the mass had a normal appearance. It was felt by the examiner that the instrument could not safely be passed by the cyst. Under novocain anesthesia, a needle was inserted posteriorly into the mass and, with difficulty, one cc. of thick white fluid was removed. This had a milky appearance and proved to be sterile when cultured.

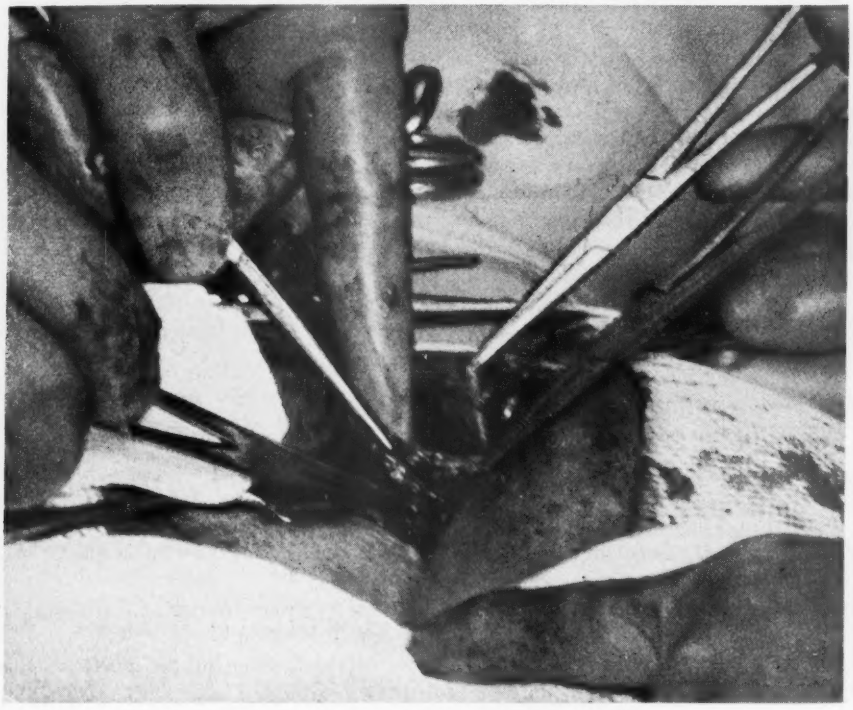

FIG. 2.—Operation showing part of cyst wall.

Roentgenologic findings: "With the rectum filled with barium, a soft tissue mass, about the size of a grapefruit, is seen to displace the lower rectum anteriorly and slightly to the left."

Operation: Under spinal pontocaine (20 mg.) anesthesia, a midline posterior six cm.-incision was made.[5] The coccyx was removed by separation of the sacrococcygeal ligaments. A large cyst, 10 x 12 cm., was easily exposed. The muscles overlying the cyst were poorly developed. The dorsal surface of the tumor was free but it was attached on the lateral surfaces and apparently inferiorly. It was seen by the operator that it could not be removed intact. Blunt dissection was continued until it ruptured and released about 200 cc. of thick, foul smelling material with large cheesy lumps and flakes. A finger was inserted into the sac and six to eight other similar but smaller cysts were identified. The cyst was not symmetrical and several small protruding pockets were identified. The dissection was then continued much in the manner that a hernial sac is stripped. The peritoneum lay superior to the mass and was not entered. On the ventral surface the rectal wall was practically continuous with the cyst. Inferiorly,

the sphincter ani internus was identified. Dissection from the rectum was facilitated by the injection of saline beneath the lining membrane of the cyst. By using this procedure bleeding was kept at a minimum. An assistant inserted his finger into the rectum and it seemed that the rectal wall was even thinner than normal. The cyst having been opened it was necessary to remove it and the smaller cysts piecemeal. Examination of the tumor disclosed no solid portions, teeth, bone or hair and one cyst, approximately 1 cm. in diameter, was sent for microscopic examination. Five Gm. of sulfanilamide were inserted in the wound. Interrupted silk was used to close the wound. The defect could not be completely closed and a small rubber tissue drain was inserted.

Pathologic Examination.—Gross: "Specimen consists of an irregular fragment of membranous tissue in which there is a cyst about 1 cm. in diameter, filled with thick coffee-colored material. *Microscopically*, the cyst is lined with stratified epithelium. No inflammatory reaction is present." *Pathologic Diagnosis:* Epithelial cyst.

With the exception of moderate difficulty in voiding and headache, her postoperative course was good. Wound dressed on 4th postoperative day and rubber tissue drain partially withdrawn, with release of 2 cc. of old blood. Three days later drain entirely removed. In all dressings care was exercised to isolate the wound from the anus. Surface of wound was dusted with sulfanilamide powder. Skin sutures were allowed to remain to the 10th postoperative day. With dressings the finger was inserted in the rectum and the site of removal was gently pressed to remove the collected fluid. The area soon decreased in size, and had the feel of the prostate gland. This rapidly disappeared and the wound was entirely healed on the 19th day, at which time she was discharged from the hospital. She was seen again one month later and had no complaints. The wound is healed and she is carrying out her duties in the W. A. C.

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BOOK REVIEW

GASTRO-ENTEROLOGY. By Harry L. Bockus, M.D. Volume I. W. B. Saunders Company, Philadelphia, 1943.

To make possible the publication of a medical book of such perfection as is exhibited in the First Volume of the proposed three volume textbook on Gastro-enterology, by Bockus, is an effort of which all concerned may be proud but for the Saunders Company to accomplish this during the chaotic times through which we are passing would seem to be making possible the impossible.

The usual quality of the paper type and binding together with that of the illustrations and the generous use of beautiful color attracts the reader at once and inveigles him into making the attempt to assimilate this exhaustive, but not exhausting, presentation of a rapidly developing specialty.

To the lay public—at least—has come an appreciation of the fact that the civilian population, as well as the Army, "lives upon its stomach," and this presentation should appear as timely to the younger members of the medical, and even to the surgical professions.

Among the many unique features of this effort is the abandonment of the present day plan of engaging large groups of authors, from many sources, for the preparation of symposia instead of the one-man authorship of textboods as in former times.

Bockus states that his collaborators have been his associates in a group who have been working together for many years in a teaching institution—The Gastro-enterological Department of the Graduate School of Medicine of the University of Pennsylvania, and as a result he believes they have developed an unusually broad interest in both medicine and gastro-enterology.

To the reviewers this attitude seems to have made possible a unity and directness of presentation of these two divisions of medicine which are usually lacking in modern medical textbooks.

Volume I deals with the Esophagus and the Stomach, devoting more than 300 pages to the problem of Peptic Ulcer.

Volume II will be concerned with the Small and Large Intestine and the Peritoneum.

Volume III will cover the subjects of the Liver, Biliary Tract, Pancreas and Secondary Gastro-intestinal Disorders.

A separate Desk Index Volume is evidence of the meticulous planning of the author which is apparent on every page of the first volume.

WALTER ESTELL LEE, M.D.

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